

BALLOON CATHETER IN ANGIOGRAPHY AND THERAPEUTIC EMBOLIZATION OF RENAL TUMOURS

An experimental and clinical study

Ragnar Jensen
med.lic., Lund



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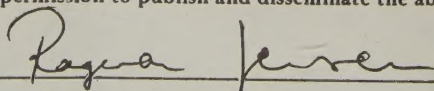
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Abstract In order to improve the angiographic results and study the circulation after occlusion of various arteries experimental investigations using balloon catheters were performed in rabbits. Occlusion angiographies visualized collaterals that were not normally opacified. The diameter of the hepatic arteries increased about 50 % and the parenchyma was better opacified. Injuries to the arterial wall were noticed and an experimental series in rabbits and dogs was performed to examine the damages. The results disclosed only a minor risk when moderate distention of 20 % of the diameter was performed. A new balloon catheter was constructed but even other balloon catheters were used for clinical examinations of the splanchnic arteries. The experimental results were also valid to clinical practice. The dilatation of normal vessels distal to the occlusion allowed visualization of small vessels in the periphery of the liver and increased the concentration of contrast medium in the parenchyma. Even small metastases near the capsule were opacified and improved judgements on operability of tumours. Dilatation of the arteries was often not observed in tumour areas and the contrast medium was shunted to the normal parenchyma. The concentration of contrast medium of a hypervascularized tumour of the liver was obviously diminished. Collaterals to tumour areas can be visualized even if they are not demonstrated by conventional angiography. Conclusions relating to the choice of tumour therapy, operation or de-arterialization and cytostatic infusion suggest that occlusion angiography is very informative and is recommended as a valuable part of tumour assessment prior to therapy. The balloon can be distended inside an artery for several hours and can thus be used for intermittent de-arterialization and for infusion of cytostatic agents. Balloon catheters make it possible to inject the embolizing material of high pressure in order to facilitate occlusion in therapy and prevent unintentional embolization. The pains associated with embolization were reduced by intraarterial injection of local anaesthetics. The painfree period was prolonged by injection through a balloon catheter.		
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This thesis is based on the following papers:

- I. Balloon catheters in angiography. An experimental investigation in rabbits.
R Jensen and T Olin
Acta Radiol Diagnosis 12, 1972, 721 - 736
- II. Complications at balloon catheter angiography. Experiments in rabbits and dogs.
R Jensen and T Olin
Acta Radiol Diagnosis 20, 1979, 593 - 605
- III. Double-lumen balloon catheter.
R Jensen and T Olin
Acta Radiol Diagnosis 17, 1976, 886 - 890
- IV. Clinical angiography with balloon catheter.
R Jensen
Acta Radiol Diagnosis 23, 1982, 93 - 105
- V. Preoperative embolization of renal tumours using balloon catheters.
R Jensen and J Nilsson
Acta Radiol Diagnosis 22, 1981, 553 - 559

Reference to these papers will be made by the numerals I - V.



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For many years angiography has been an important diagnostic tool. In early neuro- (RADNER 1951) and abdominal (BIERMAN et coll 1951) angiographies selective injections were used. In hepatic angiography, however, even injection into the hepatic artery itself sometimes failed to demonstrate tumours within the liver. In collaboration with KAUDE and WIRTANEN the author studied slow injection hepatic angiography (KAUDE et coll 1973). Using this technique, malignant nodules could be demonstrated more effectively when the earlier method had failed. The slow injection method always offered superior results in patients with hepatic tumours compared to those obtained with the rapid injection technique. However, even the slow injection method sometimes failed. In a further attempt to improve the technique occlusion angiography was used. It seemed reasonable to believe that better angiographic results could be expected when dilution of the contrast medium was minimized. This led to the experimental investigations using balloon catheters (I). The first experiments were performed on rabbits. However, there was no catheter available for this type of animal and therefore a single lumen balloon catheter was constructed and originally used.

FOSTER et coll (1970) reported damage to the vessel wall after the use of a Fogarty catheter but otherwise there were few reports of vascular damage resulting from the use of balloon catheters.

Before clinical examinations could be performed an evaluation of such complications was therefore undertaken. The experimental technique was similar to that used in clinical occlusion angiography.

A flow-guided balloon catheter for experimental haemodynamics had already been described by DOTTER and LUKAS in 1951. NORDENSTRÖM (1962) produced single lumen balloon catheters for clinical use. During 1970 WHOLEY et coll presented a catheter designed for clinical

practice and GOPALRAO et coll (1972) used this catheter to control haemorrhage and during operation for embolectomy and angiography. The type of plastic (polyvinyl) used has a poor "memory", i.e. the catheter does not retain the preformed curve after being straightened out during introduction into the blood vessel. The catheter was therefore reinforced with a steel thread cast into the wall. This arrangement, however, seemed to be too stiff for several types of angiography. During the dog experiments it became apparent that a double-lumen balloon catheter made of polyethylene, suitable for introduction using the Seldinger technique, was needed for clinical practice. Such a catheter was developed in collaboration with A/S Surgimed in Denmark (III).

During the 70's interest in occlusion angiography increased (REUTER 1970, WHOLEY et coll 1970, WEBER 1979, 1980) and suitable catheters then became available. A 7F balloon catheter with good finish (Medi-Tech) was used during the last part of the clinical studies.

The aim of the experimental studies dealing with occlusion angiography in rabbits and dogs included:

1. Study of the circulation in the splanchnic arteries during arterial occlusion,
2. Examination of the concentration of contrast medium in the vessels and parenchyma,
3. Investigation of any damage to the arterial wall following distention by the balloon,
4. Determination of a safe upper limit to the degree of distention.

The aim of the clinical studies was to:

- a. Develop a catheter for percutaneous insertion into the vessel. The catheter should be shaped for selective examination.
- b. Examine the wall of the artery after distention of the balloon.
- c. Evaluate the risks of occlusion angiography.
- d. Study whether occlusion angiography could reveal pathologic changes more effectively than conventional angiographic techniques.
- e. Investigate whether a balloon catheter could change the hepatic circulation in a way that is suitable for therapy.
- f. Demonstrate the existence of collateral circulation after occlusion of an artery.
- g. Examine the means by which balloon catheters might facilitate embolization.
- h. Judge the effect of an anaesthetic agent injected through a balloon catheter during embolization of a kidney.

MATERIAL AND METHODS USED IN EXPERIMENTAL INVESTIGATIONS

Balloon catheter angiography in rabbits and dogs

The first study comprised angiography in 25 rabbits (I). The animals were anaesthetized with barbitone sodium (Mebumalnatium, ACO, Sweden). The catheters were introduced by a cut-down technique from the femoral and the carotid arteries and the right superficial jugular vein. Selective angiography was performed and occlusion angiography was then achieved using a home-made single lumen balloon catheter of polythene.

Contrast medium (Isopaque Cerebral, Nyegaard & Co AB) was injected into adjacent vessels by another catheter with or without

vessel occlusion. The visceral, renal and cerebral circulations were studied.

The experimental study (II) which evaluated the complications of balloon catheter angiography was performed in 6 rabbits and 6 dogs under general anaesthesia (Pentobarbitone sodium). In the rabbits the same contrast medium and catheter were used as in the first study. In dogs Isopaque Cerebral was employed for selective angiography and Isopaque Coronar for aortography.

The reason for using dogs for experiments (II) was twofold: The arteries were big enough for catheters manufactured for human use, and the volume of the balloon was large enough to avoid over-distention at injection by hand.

The balloon catheter was a double-lumen catheter size 7.5 F from Edward's Laboratories. Aortography was performed via a catheter (Ödman-Ledin, Kifa, Sweden, OD/ID 1.8/1.2 mm) introduced into the femoral artery.

The balloon was inflated within the visceral and renal arteries for 2 minutes. Aortography and selective angiography were performed immediately after deflation of the balloon. Repeat angiography was performed 2 - 12 weeks later. The diameter of the vessels during and immediately after distention by the balloon was measured on the films with a magnifying glass with a scale graduated in 0.1's of a millimetre. The distention of the arteries was calculated and adjusted for magnification and the margin of error in the measurements was estimated. After repeat angiography the animal was sacrificed and the occluded renal and splanchnic arteries were removed for microscopy at the Department of Pathology, University Hospital in Lund.

EXPERIMENTAL RESULTS

Visceral circulation and collaterals during balloon occlusion in rabbits (I).

Collaterals that are not normally visible between the coeliac and superior mesenteric artery could be visualized when occlusion of one artery and injection into the other was performed. The diameter of the common hepatic as well as the proper hepatic artery increased by about 50 % when the superior mesenteric artery was occluded. Even the size of the arteries in the periphery increased and small vessels between branches of the main arteries were opacified. The increased quantity of contrast medium in the liver arteries resulted in better opacification of the parenchyma and improved the venous phase.

When the coeliac axis was occluded and the superior mesenteric artery injected, the calibre of the mesenteric artery and its branches did not change and collaterals to the coeliac axis were usually demonstrated.

Complications due to balloon occlusion of an artery (II).

The occlusion angiographies in rabbits revealed that the balloon could damage the wall of an artery. In one case all 3 layers were injured by over-distention. The lesion was usually more extensive in relatively small vessels, such as the renal arteries compared to larger vessels such as the superior mesenteric artery. In small vessels little margin exists between adequate occlusion and over-distention of the balloon. Dilatation of the artery was sometimes evident and on one occasion very strong spasm was noted distal to the dilatation. Repeat

angiography 12 weeks later demonstrated regression of the dilatation and microscopically some degree of healing was noticed.

In the dog as in the rabbit experiments, over-distention was more likely to occur in small vessels such as the renal arteries. Dilatation of the artery was evident in 8 of 18 vessels immediately after balloon distention but at repeat angiography 2 - 12 weeks later a small widening remained in only 3 vessels. Microscopy of the vessels revealed extensive injury to the internal elastic lamina and to the tunica media. In all the remaining vessels except one no injury or only a small lesion of the internal elastic lamina was noticed at microscopy. Only one vessel that looked normal on the repeat angiogram was found to have sustained damage to the internal elastic lamina and to the tunica media. Injury of the adventitia was not encountered in any of the experiments in dogs. Vascular injury due to the balloon catheter employed in these studies was not common in arteries with an internal diameter of 4 mm or more if the increase in diameter of the vessel did not exceed 20 %. No stenosis of the arteries developed during the period between dilatation and repeat angiography 2 - 12 weeks later. One experiment in a rabbit disclosed injury to the internal elastic lamina secondary to preparation for microscopy.

MATERIAL AND METHODS IN THE CLINICAL INVESTIGATIONS

A balloon catheter designed for angiography (III).

A double-lumen balloon catheter of low-density polyethylene was developed in collaboration with A/S Surgimed in Denmark. The balloon was made of latex and fixed to the catheter by 2 small rings of heat-shrinkable polyethylene. The outer diameter of the catheter was 2.5 mm except for the part near the balloon where it measured 3.0 mm. The Seldinger technique for percutaneous insertion was used.

The catheter is disposable and it is not possible to sterilize it in benzalkonium chloride or similar solutions since these will destroy the balloon.

Material and technique used in clinical occlusion angiography (IV).

Fifty angiographic examinations of abdominal vessels were performed with an ordinary polyethylene catheter (7 F) (IV). Repeat angiography was performed using a double-lumen balloon catheter. In the first 33 examinations a catheter from A/S Surgimed was used and in 17 investigations a 7 F catheter from Medi-Tech was used. The age of the patients varied from 27 to 81 years. The diameter of the vessels was measured directly on the films from the first angiography and the degree of balloon inflation needed to occlude the vessels was determined. The diameter of the balloon was about 20 % greater than that of the vessel due to the magnification on the films. The catheter was moulded in hot water and the manoeuvring channel to the balloon was situated in the minor curve. If this channel happens to be located on the outer curvature the channel may become kinked thereby making deflation of the balloon almost impossible when the catheter is straightened out in a vessel. The routine technique for percutaneous insertion was used. The balloon was expanded with contrast medium of low viscosity during fluoroscopy in order to control the size and shape of the balloon. A deformation of the balloon was noticed when it reached the wall of the vessel.

The mean injection rate of contrast medium during conventional angiography of the coeliac and hepatic artery was about 6.6 ml/s and of the superior mesenteric artery about 8.3 ml/s. The amount of contrast medium injected was 45 ml into the coeliac and hepatic arteries and 50 ml into the superior mesenteric artery. Occlusion angiography was performed using roughly the same rate of injection.

Embolization with balloon catheter in renal tumours (V) .

Transcatheter preoperative embolization of 13 patients with renal tumours was performed. The size and vascularization of the tumour was demonstrated by nephroangiography. Several days later embolization was performed.

Three types of balloon catheter, manufactured by Edward's Laboratories, California, USA (WHOLEY et coll 1970), or A/S Surgimed, Denmark (III), or Medi-Tech, Massachusetts, USA (WHOLEY 1977) were used.

Surgicel (Ethicon Ltd), a sterilized oxidized cellulose (polyanhydroglucuronic acid) was used as the embolizing material. It was cut into pieces by hand. Microscopic examinations of the pieces revealed threads of a diameter of 40 μ and of a smallest length of 40 μ .

The embolization procedure started with an ordinary catheter with its tip placed well within the renal artery. Pieces of Surgicel mixed with physiologic saline were injected. When the circulation was blocked peripherally the catheter was withdrawn and the balloon catheter introduced. With the catheter in the renal artery the balloon was expanded and embolizing material injected. The renal artery and its branches were occluded. During and after the procedure with the balloon remaining inflated, 2 - 4 ml Lidocaine 2 % (Xylocain, Astra) were injected several times in an attempt to relieve pain. The degree of balloon inflation and the duration of occlusion were varied. The width of the renal arteries and the increase of arterial diameter when the balloon was inflated were measured. After nephrectomy microscopic examination of the renal artery was performed.

RESULTS OF THE CLINICAL STUDIES

Use of the double-lumen catheter from A/S Surgimed.

The superior mesenteric, coeliac and hepatic arteries were catheterized. The catheter could also be used for embolization of the renal artery. The calibre is somewhat larger than that of ordinary single lumen catheters and a widening of the puncture hole with another catheter (Medi-Plast 2, soft grey, OD/ID 2.8/1.4 mm) was sometimes necessary. Only one complication was recorded. A patient (69 years old) developed a haematoma in the groin 12 days after angiography. The haematoma was evacuated and the puncture hole in the femoral artery was sutured. Recovery was uneventful. The surgeon noted that an atheromatous plaque had been punctured.

Complications due to the balloon in occlusion angiography and embolization.

After dilatation of the visceral arteries by about 20 % during balloon catheter angiography repeat angiography did not reveal any signs of vascular damage. No thrombosis was noticed in the arteries and no clinical signs of embolus in the legs were observed.

Microscopic examination of the renal arteries after increase in diameter of about 20 % revealed damage only to the internal elastic lamina in a few cases. No damage could be seen in the tunica media or adventitia. Even when the balloon was kept inflated for as long as 11 hours no serious damage was seen.

Occlusion angiography of the liver

Occlusion of the hepatic artery and injection of contrast medium distal to the occlusion caused opacification of small vessels in the periphery when the injection rate was high enough to prevent dilution (balanced injection rate) with blood from collaterals. Metastases in the periphery of the liver, which were not opacified at conventional angiography, became visible during occlusion angiography. The arterial phase was prolonged in tumour areas compared with normal parenchyma. This made it possible to outline the borders of a tumour more precisely.

When the injection rate was too low to balance the blood from collaterals the contrast medium in the arteries and parenchyma became diluted by this blood. Occlusion angiography using a slow injection rate gave less information than conventional angiography.

Dilatation of the normal vessels of the liver distal to the occlusions was observed. The amount of contrast medium in normal parenchyma was increased and vessels in the periphery were opacified. The change in calibre of vessels providing the main blood supply to the tumour and those within the tumour itself showed no or only minor increases in calibre. The concentration of contrast medium within a tumour at a location close to the hilum was sometimes diminished. Conventional angiography achieved better opacification of hypervascular tumours in the hilum of the liver but tumours in the periphery were often only opacified during balloon catheter angiography. Occlusion angiography was associated with prolonged arterial, parenchymal and venous phases. This delay in passage of the contrast medium was accentuated within tumours.

Demonstration of collaterals

Occlusion together with injection of contrast medium into an adjacent vessel revealed collaterals that were not seen during conventional angiography.

Collaterals could also be opacified when the injection rate distal to the occlusion was sufficiently high (over-balanced) thereby forcing the contrast medium through the vessels.

Balloon catheter at embolization

Embolization with the balloon catheter prevented reflux of embolic material into the aorta. The injection could be made at a high pressure in order to fill the arteries with embolic material also in the periphery. Cautious emptying of the balloon allowed one to observe the contrast medium that had been injected, pulsating in the renal artery. This was a sign of complete embolization.

The balloon catheter made it also possible to force Lidocaine into the embolized area thereby resulting in a prolonged period of analgesia. A further 20 patients have been successfully treated since (V) was published. When the pain returned, usually after 1 - 12 hours, a further injection was given and again immediate pain relief was obtained. The duration of the period of pain relief seemed to be shorter after each repeat injection and eventually morphine administration was necessary.

DISCUSSION

Catheter complications in clinical use

Complications following percutaneous catheterization of the femoral artery have been reported by several authors. It has been suggested that thrombosis can be initiated by spasm (ERIKSON and JORULF 1970), by withdrawal of a catheter coated with thrombocyte clots (NEJAD et coll 1968, JACOBSSON 1969), or by mechanical injury to the endothelium (FELLOWS 1972, MORTENSSON et coll 1975). Several types of complications have been described by SIGSTEDT and LUNDERQUIST (1978) and HESSEL et coll (1981).

Apart from those complications mentioned above it appears that mechanical distention and occlusion of the artery by the balloon catheter itself may be of importance. Inflation of the balloon did not cause inconvenience to the patients and no ischaemic pain was registered during the angiographies. The occlusion of the vessel was shorter than 2 minutes. Some patients experienced a slightly increased feeling of heat compared with ordinary angiography. That finding was probably due to less dilution of the contrast medium during occlusion angiography. WEBER and NOVAK (1980) reported, however, a slight feeling of local pain during short balloon blockade. The discomfort ceased immediately after removal of the balloon.

The Fogarty balloon catheter has been used for many years as an embolectomy catheter and complications have been reported in this context also. FOSTER et coll (1970) described 4 types of complication: Rupture of the artery by the inflated balloon, perforation of the artery by the tip of the catheter, tear or disruption of the intima and rupture of the balloon with embolization of a fragment of rubber. The Fogarty catheter is stiff and not designed for use in angiography but the injuries due to the balloon are valid also for angiographic balloon catheters. BURGNER et coll (1981) used angiographic balloon catheters (Medi-Tech)

in dogs. The rate of injection of contrast medium was 8 - 10 ml/s and disruption of the wall separating the two lumina of the catheter occurred twice. This resulted in a rapid, damaging inflation of the balloon during angiography. No such complication was observed in the present study. However, the injection rate used here did not exceed 8.8 ml/s.

The walls of the balloon catheter (Medi-Tech) are thin and easily penetrated by a guide-wire. If the catheters have been moulded so that the injection channel is located on the outer curvature penetration by the guide-wire is more likely via the outer wall rather than via the intervening septum. The risk of uncontrolled inflation of the balloon when contrast is injected is thus eliminated. BURGNER et coll (1981) also reported that in 20 cases of angiography in the superior mesenteric artery, balloon deflation was impossible in 2 cases. When the catheter is bent as mentioned the balloon was deflated without difficulty. The manoeuvring channel should thus be on the inner and the injection channel on the outer curve of the catheter. Contrast medium of low viscosity was used to inflate the balloon.

WEBER (1980) and WEBER and NOVAK (1980) using a Swan-Ganz balloon catheter occasionally observed arterial spasm which disappeared immediately after desufflation of the balloon. Spasm was not observed in any of the present clinical studies, but was sometimes noticed in the experimental studies in rabbits (II).

No perforation of the vessels by the balloon catheter was observed. BURGNER et coll (1981) recorded one case of perforation of the superior mesenteric artery in an experimental study on 20 dogs. Because of the different types of complication that may arise, they concluded that balloon occlusion angiography should only be performed by experienced angiographers (BURGNER et coll 1981). The advantages should clearly outweigh the risks. This is in agreement with the experimental investigations of JEKELL et coll (1980).

Damage to the muscular component of the media was observed by CASTANEDA-ZUNIGA et coll (1982) after intraluminal balloon angioplasty in dogs and rabbits. This supports the results obtained in the present study in the animal experiments after over-distention of the balloon. However, this was not seen after moderate distention of the balloon in the clinical investigations. Electron microscopic studies on dogs have demonstrated extensive fragmentation of the muscle cells of the tunica media immediately after distention of the artery by 50 % using a Grüntzig balloon catheter. The muscle cells were replaced by collagen two months later and the vessels had thus lost the ability to react to stimuli (CASTANEDA-ZUNIGA et coll 1980, 1982).

WEBER and NOVAK (1980) performed microscopic examinations in 5 patients after 2 hours of carefully performed occlusion of the renal artery. No damage of the intima of the renal arteries was observed. This is in agreement with our observations that no serious damage occurred when the increase in diameter of the arteries did not exceed 20%. The duration of occlusion in our material varied from 2 minutes to 11 hours.

A balloon catheter can thus be used for temporary occlusion and infusion of cytostatic agents for several hours without risk of damage to the artery.

Circulation during occlusion angiography and therapeutic implications

Intraarterial infusion chemotherapy and ligation of the hepatic artery have been utilized for several years to treat tumours of the liver (FORTNER et coll 1973, KOUDAHIL and FUNDING 1972, ALMERSJÖ et coll 1976). In order to avoid the deleterious effects of hepatic artery ligation on normal liver tissue at operation and prevent new collaterals opening up to supply a liver tumour a technique for intermittent

but complete interruption of the hepatic artery has been developed (BENGMARK et coll 1974, FREDLUND and BENGMARK 1975). At operation two thin polyethylene slings were placed around the hepatic artery, one distal and the other proximal to the gastroduodenal artery. The slings were drawn out through the abdominal wall and an infusion catheter was placed in the gastroduodenal artery with its tip lying in the hepatic artery between the slings. Infusion of cytostatic drugs was performed during occlusion (BENGMARK et coll 1978, 1980, DAHL et coll 1981).

Other methods for intermittent occlusion have been used (EL-DOMEIRI 1976, EL-DOMEIRI and MOJAB 1978). At operation a balloon catheter was introduced into the gastroepiploic artery and the tip was positioned in the hepatic artery. The end was brought out onto the skin through an incision in the right hypochondrium. Occlusion was maintained for 45 to 60 minutes twice daily for a period of 3 weeks. Preservation of the integrity of the small blood vessels within and around the tumour and resumption of the arterial flow facilitates diffusion of the cytostatic agents into the neoplastic cells. Heparine (5,000 USP) was given intravenously to prevent intraarterial clotting.

Intermittent occlusion of the hepatic artery by means of a balloon catheter can also be performed using a percutaneous angiographic technique (IV). The balloon can even be located distal to the main hepatic artery and the catheter can be left in situ for 11 hours or more. Since article (V) was published 20 more patients have been embolized using a balloon catheter with an occlusion time lasting as long as 20 hours; there was no clinical evidence of complications. BENGMARK and FREDLUND (1978) postulated that occlusion lasting 8 - 12 hours should be sufficient to produce optimal tumour necrosis. De-arterialization is known to extend the central necrosis of liver tumours, reduce the number of malignant cells and reduce the tumour burden on the patient (McDERMOTT et coll 1978, MORI et coll 1966). There is no reason to believe that balloon occlusion should be less effective than intermittent

occlusion by the method of BENGMARK and FREDLUND (1978) or permanent occlusion.

After de-arterialization of a liver tumour viable malignant cells will still remain in the periphery (ALMERSJÖ et coll 1966, WILLIAMS and MELIA 1980). There appears to be little effect on the outer zone when there is a well developed vascular plexus and rapidly multiplying cells (ALMERSJÖ et coll 1972, RAMMING et coll 1976). Treatment with oncolytic drugs can then be performed (KOUDAHL and FUNDING 1972, FORTNER et coll 1973, ALMERSJÖ et coll 1976), administration being by the theoretically ideal route namely intraarterially (BENGMARK and FREDLUND 1978). A cytotoxic preparation can be highly effective in killing malignant cells but before operation or before cytostatic infusion an extensive angiographic examination should be performed in order to show the vascularity and delineate the boundaries of the malignant lesion. Coeliac and hepatic angiography have been used as pre-operative investigations but do not reveal metastases in the periphery and often give an incomplete delineation of liver tumours.

Balloon catheter angiography opacified metastases at the periphery of the liver and gave better information about operability than conventional angiography. Even tumours near the capsule were visualized.

Occlusion of the hepatic artery before contrast medium injection revealed dilatation of normal vessels (IV). BAYLISS (1902, 1923), HIROSE and SCHILF (1931), and FOLKOW (1949, 1952) showed that reduction of the blood pressure by occlusion elicits vasodilatation. This was demonstrated in the normal human liver (IV). In areas with heavy tumour involvement no increase in vessel calibre was observed. A tumour induces formation of collagen in the surrounding tissue (PIETRO and GRANTHAM 1963, MARIONS and WIECHEL 1974, EKELUND et coll 1977). The collagen content of hepatomas in rats and mice was measured by GULLINO and GRANTHAM (1962). They showed that all the hepatomas studied contained more collagen than normal liver. The colla-

genous stroma of the tumour is considered to be a product of the host's fibroblast reaction to the tumours (GULLINO et coll 1963). On the other hand, mesenchymal tumour cells such as osteosarcoma and chondrosarcoma are considered to produce large amounts of collagenous matrix (GAY and MILLER 1978). Malignant cells influence the connective tissue of the host so that the normal collagen is destroyed and a new type is formed. The newly formed connective tissue stimulates formation of new malignant cells (LEBEDEV 1979).

The large amount of collagen and malignant cells in a tumour make the tissue turgid. This may explain why the arteries may not dilate after occlusion even in the absence of obvious infiltration of the vessels.

Alteration in the circulation of the liver following hepatic artery occlusion causes a diversion of the injected contrast medium or cytostatic agent into the normal parenchyma. Conventional angiography gives a false picture of the distribution of cytostatic drugs after occlusion of the artery. Balloon catheter angiography with a low injection rate on the other hand gives better information. The true circulation can, however, not be visualized. Contrast medium induces chemical vasodilatation (AMUNDSEN et coll 1956, DELIUS and ERIKSON 1969, BOIJSEN et coll 1971, LEVIN 1978, NYMAN et coll 1980).

Tumour vessels do not differentiate in the normal way into arterioles or venules despite the fact that they are larger than capillaries (ALGIRE et coll 1945, BILLING and LINDGREN 1944, LAGERGREN et coll 1960, 1961). The walls of such vessels consist only of a single layer of endothelium (EKELUND et coll 1977, SIMMONS et coll 1977) and no dilatation can be expected after occlusion due to the absence of muscle cells.

The circulation after occlusion must be altered in order to make infusion of cytostatic agents more effective. Vasopressin seems to be

suitable: Vasoconstrictor response to vasopressin in the peripheral hepatic arteries decreases the accumulation of contrast medium in normal liver tissue (BOIJSEN and GÖTHLIN 1980). The contrast medium is thus diverted to the liver tumour after injection of this drug. After a short period of time the effect is reversed in spite of continued infusion at high dosage (HANSON 1970, BARR et coll 1975, SIMMONS et coll 1977). The beneficial effect of vasopressin thus is reversed and becomes unfavourable. Opacification of hepatic tumours can be improved by injection of vasoconstrictor drugs such as Angiotensin (EKELUND and LUNDERQUIST 1974) or Epinephrine (BOIJSEN and REDMAN 1967) during angiography. The drugs could be combined with a cytostatic infusion (IWAKI 1980), but the effect of Angiotensin lasts only one or two minutes (KAPLAN and BOOKSTEIN 1972). One way to get a better result from infusion of cytostatics is to place the tip of the catheter more selectively. An alternative method of temporarily blocking the hepatic artery flow with degradable microspheres combined with oncolytic drugs has been used to treat secondary liver tumours (ARONSEN et coll 1979).

Collateral circulation

Occlusion of a vessel causes a reduction of the intravascular pressure. As a result the direction of flow in collaterals is diverted towards the area supplied by the occluded vessel. Several anastomotic pathways to the human liver have been demonstrated. MICHELS (1953, 1960, 1966) demonstrated 26 possible collateral routes to the liver. Ten of these represented, however, anatomic variations (PETTERSSON 1975). SEGAL (1923) noted that when one lobar artery was perfused the contrast appeared in the other lobar artery even when perfusion pressure was insufficient to cause capillary or arteriolar filling. He concluded that pre-arteriolar anastomoses existed between the two lobes. On the other hand MAYS and WHEELER (1974) on cadaver liver reported no cross-filling to the other hepatic lobe when one lobar artery was perfused. Collaterals in the liver hilum between the hepatic arteries were observ-

ed in patients with occlusion of the main trunk (REUTER and OLIN 1965, ALMÉN 1966, REDMAN and REUTER 1970, KOEHLER et coll 1975).

Some collaterals are open even if no occlusion is performed though they may not be demonstrable during conventional angiography. The flow and pressure will rise significantly in an arterial tree when the parent vessel is injected selectively. Direction of flow, as seen on the arteriogram, might be the reverse of that which occurs under physiological conditions (LEVIN 1978). It is thus important to perform a control examination mimicking the conditions following de-arterialization, whether permanent or intermittent, when infusion of cytostatics is planned. Different collaterals seem to open up progressively and can take over the circulation to a tumour at various times. A low injection rate sometimes fails to visualize a tumour as the contrast is swept away by blood from the collaterals (IV, Fig. 7) but will show the direction of flow of a cytostatic agent after de-arterialization.

Hilar collaterals exist (REDMAN and REUTER 1970, GRABBE and LANGE 1981) and increase in size instantly following arterial occlusion (CHUANG and WALLACE 1980). TYLÉN et coll (1981) observed collaterals from the inferior phrenic arteries during hepatic artery occlusion. Many authors have observed collaterals to the liver at different periods after de-arterialization. WILLIAMS and MELIA (1980) observed the existence of a collateral circulation within 4 to 6 weeks. LOUGHRIDGE et coll (1968) observed myriads of small collaterals within one week. PLENGVANIT et coll (1972) reported that collaterals developed as early as one week after ligation and were progressively enlarged. BENGMARK and ROSENGREN (1970) noticed re-establishment of the arterial circulation via collaterals 4 days after operation.

Others (KOEHLER et coll 1975) have observed the development of collaterals after 4 hours, and repeat angiographies revealed increasing size during the 6 months after surgery. The flow passes from a high

to a low pressure system and the site of ligation influences the pattern of collateral vessels which then develop.

Occlusion with a balloon catheter and injection distal to the balloon did not opacify collaterals to the occluded area if the injection rate was low or balanced. When the injection rate was high or over-balanced the collaterals could be visualized (IV). CAREY et coll (1980) studied the canine hind limb. The collateral circulation was poorly visualized in non-selective distal aortograms. He concluded that selective injection directly into the collateral donor artery improved the demonstration of the collateral circulation which was best seen after balloon occlusion arteriography of the collateral donor vessel. I believe, however, that it is better to occlude the supplying arteries and then perform a selective injection into the arteries that are supposed to emit the collaterals.

Most solid tumours seem to be capable of surviving by simple diffusion of nutrients until they reach a diameter of a few millimeters. In the avascular stage tumours remain dormant (FOLKMAN 1974). The tumour cannot grow further without a blood supply from new capillaries. Tumour cells appear to stimulate endothelial cell proliferation and endothelial cells may have an indirect effect upon the rate of tumour growth (FOLKMAN 1971). The capillary proliferation is stimulated by a tumour angiogenesis factor released by the tumour. The factor is a protein with a molecular weight of approximately 100,000 and diffuses over a distance of at least 3 - 5 mm (FOLKMAN 1974). Experiments support the opinion that tumours themselves cannot produce capillaries. New vessels arise from the host and grow into the tumour (CAVALLO et coll 1972, GIMBRONE et coll 1973). Thus a tumour can stimulate the growth of vessels from regions that normally do not supply collaterals. These parasitic vascular connections, deriving from neighbouring organs and tissues, are supplemental to the normal vascularization. Their existence is essential for both diagnostic angiography and treatment of abdominal masses (HIETALA and KUNZ 1979, LAMARQUE et coll 1981, BRAC-

KEN and JONSSON 1979). These vessels can only be eliminated by peripheral embolization.

An extensive angiographic examination must be performed prior to operation or infusion and occlusion angiography should be included.

Embolization as a therapeutic method

Transcatheter embolization has been recommended by several authors but complications due to "spill-over" have been reported (EKE-LUND et coll 1979, TEGTMEYER et coll 1977, HABIGHORST et coll 1978, WALLACE et coll 1981, WOODSIDE et coll 1976, GANG et coll 1977, TADAVARTHY et coll 1974, LEVIN et coll 1980, TISNADO et coll 1979). This complication can be eliminated by the use of a balloon catheter. No unintentional embolization was noted in agreement with the technique of WEBER and NOVAK (1980). Furthermore, a balloon catheter makes it possible to inject the embolizing material at a high pressure without reflux (STRECKER et coll 1979) and it is possible to force the material out into the periphery.

Several different types of embolic material have been used, including tissue pieces (BROOKS 1930), autologous clots (RÖSCH et coll 1972), homogenates (ALMGÅRD et coll 1973), dextran (LALLI et coll 1969), Bucrylate (LUNDERQUIST et coll 1978, EKELUND et coll 1979). Spongostan (TURINI et coll 1976, EKELUND et coll 1979), gelfoam (GOLDSTEIN et coll 1975, 1976, BERGREEN et coll 1977), ethanol (ELLMAN et coll 1980, 1981, EKELUND et coll 1981), detachable small balloons (SERBINENKO 1974, GRINNELL et coll 1981) and degradable microspheres (ROTHMAN et coll 1976). All these have been used for embolization of the periphery.

Coils (GIANTURCO et coll 1975, WALLACE et coll 1976) facilitate a proximal occlusion which is almost a definitive occlusion but intra-hepatic collaterals develop instantaneously when this type of hepatic embolization is performed (CHUANG and WALLACE 1981, KOEHLER et coll 1975).

Peripheral embolization prevents re-vascularization from collaterals (ATHANASOULIS 1980) and should be performed to create a complete ischaemia of the liver tumour.

Renal and hepatic vascularization differ, but peripheral embolization of the renal arteries is necessary to achieve necrosis. ADLER et coll (1978) have concluded that the embolic material must occlude the interlobular arteries to cause necrosis of the renal parenchyma since peri-capsular arteries may form communications.

When parasitic blood supplies from adjacent organs (HIETALA and KUNZ 1979, LAMARQUE et coll 1981, BRACKEN and JONSSON 1979) exist it is necessary to embolize at a point distal to the interlobular arteries near the capsule.

The particle size is crucial for successful peripheral embolization. The patency of the portal vein is of the utmost importance because it is the basis of an embolization route to the liver. The oxygen content of the portal blood is sufficient to maintain the metabolic function of the liver (McDERMOTT et coll 1963) and prevent infarction of the parenchyma. The embolic material may not reach the hepatic sinusoids (CHUANG and WALLACE 1981) or pass arterio-portal anastomoses (MITRA 1966). BURGNER and GÖTHLIN (1978) performed angiographic, microangiographic and histological examinations of rabbits and suggested that intrahepatic arteries of less than 200 μ diameter are at least functional end-arteries since scattered infarcts and no intrahepatic collaterals were observed post embolization.

Permanent embolization of the hepatic artery and its branches in pigs as far as the arterioles has been shown to induce hepatic infarctions (WHITE et coll 1977). Experience with Ivalon particles has indicated that peripheral occlusion of the hepatic arteries using particles of 250 μ to 590 μ diameter is well tolerated by the patients (CHUANG et coll 1981). Microspheres and silicone of 175 μ diameter caused severe liver

dysfunction, hepatic cyst and abscess formation in animal experiments (DOPPMAN et coll 1978).

Clinical experience (CHUANG and WALLACE 1981) suggested that the human tolerates embolization by particles as small as 250μ which seem to be smallest usable particle size. Microscopic examination of Surgicel cut into small pieces revealed threads of very different sizes. The smallest had a length of 40μ and a diameter of 40μ . It is thus possible that these pieces may be too small and not suitable for hepatic embolization.

Post embolization syndrome

The clinical sequelae following ischaemia after occlusion of the renal artery comprise pain, nausea, vomiting and fever (WALLACE et coll 1981) and all these symptoms were observed in this study. Flank pain originating from the kidney usually begins during the embolization procedure. Some authors have described it as "slight to moderate" (WEBER and NOVAK 1980, ALMGÅRD et coll 1973). Others (EKELUND et coll 1979, WOLF 1979, PROBST et coll 1980, WALLACE et coll 1981, GOLDSTEIN et coll 1975) have characterized it as "intense or severe" but analgesics, including narcotics, were sufficient to relieve the pain. Narcosis (HABIGHORST et coll 1977) and continuous epidural block (GÖBEL et coll 1978) were thought to be the best methods of anaesthetic management. Intraarterial injection of analgesics via the catheter has been used (HLAVA et coll 1976, REISEGGER et coll 1977, PARRIS et coll 1981) with good results at the beginning of the embolization but analgesics had to be added again after 2 - 5 hours.

This is in agreement with our results but a prolonged effect was noticed after forceful injection through the balloon catheter. The local anaesthetic was pushed into the periphery between the wall of the artery and

the embolic material. Repeat injection of 3 - 4 ml 2 % Lidocaine was made several times at an interval of 2 - 12 hours and an immediate result was always obtained. The painfree period was, however, shorter and shorter and after about 6 - 12 hours analgesics were added. This short effect might be a sign of successful embolization and proves that the local anaesthetic could no longer be pushed into the renal parenchyma. It was often noticed that the balloon was forced back into the aorta during the injection.

There are, however, other factors that might influence the effect of local anaesthesia. The drugs block conduction of impulses in nerve fibres without depolarizing the membrane (TOMAN 1952). The membrane is stabilized by some mechanism so that the threshold for depolarizing is elevated. The drugs interfere with the permeability to both sodium and potassium and the most important effect is probably on the transient increase in sodium permeability following a slight depolarization of the nerve membrane (RITCHIE and GREENGARD 1966). It is believed that the non-ionized fraction of the local anaesthetics penetrates the nerve membrane, although the cationic form is required for local anaesthetic activity within the cell (RITCHIE and GREENGARD 1961). During embolization the anoxia produces an acidic pH in the tissues and acidic pH results in a preponderance of the ionic form of the drug: Therefore, penetration of the nerve membrane would be lessened and anaesthesia would be poor (MEDICAL PHARMACOLOGY 1972). Furthermore, experiments have revealed that anoxia reduces the action potential of the nerve fibre during the relative refractory period (WINTON and BAYLISS 1955) and the number of impulses through a nerve can be increased.

The nerves to the kidney form a rich plexus of filaments from the coeliac plexus and the upper end of the aortic plexus. They accompany the renal artery and continue into the kidney around the branches of the renal artery to supply the vessels and the renal glomeruli and tubules (GRAY's anatomy 35th ed., 1973). Vasa nervorum may reach the nerves proximal to the embolized renal artery and may be intact even if the re-

nal parenchyma is damaged. When the cells of the kidney are damaged the potassium ions pass the cell membrane and the concentration outside the cells is increased. The high concentration can elicit a depolarization not only at the nerve endings but also everywhere on the axon or the cell body (HAEGERSTAM 1982). The local anaesthetic injected into the renal artery might not reach the site of depolarization and can thus not stabilize the nerve membrane.

GENERAL SUMMARY AND CONCLUSIONS (I - V)

The experimental part of this study has shown that occlusion angiography made possible visualization of collaterals between the coeliac and superior mesenteric artery that were not normally opacified. The diameter of the hepatic arteries increased about 50 % in diameter. Small vessels in the periphery were visualized and the parenchyma of the liver was better opacified.

Vascular injury to all three layers of the arterial wall by overdistention of the balloon was sometimes noted. There was, however, only a minor risk when moderate distention (about 20 % of the diameter) was performed. Injuries were more common in arteries with a diameter of less than 4 mm.

The clinical part of this study has revealed that the experimental results were also in many ways valid to clinical practice. The dilatation of normal vessels distal to the occlusion allowed visualization of small vessels in the periphery and increased the concentration of contrast medium in the parenchyma. Even small metastases near the capsule of the liver were opacified which improved the determination of operability.

Dilatation of the arteries was often not observed in tumour areas and the contrast medium was thus shunted to the normal parenchyma. The concentration of contrast medium of a hypervascularized tumour of the liver was obviously diminished.

Conclusions relating to the choice of tumour therapy, operation or de-arterialization and cytostatic infusion, suggest that occlusion angiography is very informative and is recommended as a valuable part of tumour assessment prior to therapy.

Collaterals to tumour areas can be visualized by occlusion angiography even if they are not demonstrated by conventional angiography. Elimination of collaterals is important when de-arterialization of a tumour is performed.

A moderate distention of the balloon inside an artery can be made for several hours without serious damage to the walls of the vessel.

It is concluded that balloon catheters can be used for intermittent de-arterialization and for infusion of cytostatic agents. Balloon catheters make it possible to inject the embolizing material at high pressure in order to facilitate occlusion in the periphery and also prevent unintentional embolization.

The pain associated with post embolization syndrome was reduced by intraarterial injection of local anaesthetics. The painfree period was prolonged by injection through a balloon catheter.

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BALLOON CATHETERS IN ANGIOGRAPHY

An experimental investigation in rabbits

by

R. JENSEN and T. OLIN

Small balloon catheters of reliable quality and suitable for percutaneous introduction into human blood vessels have recently been developed (NORDENSTRÖM 1962, WHOLEY et coll. 1970). A general survey in animals of the possible application of such catheters to roentgenology was consequently considered timely.

Material and Methods. Twenty-five rabbits were anaesthetised with intravenous pentobarbitone sodium (Mebumalnatrium, ACO, Sweden). Various catheters were introduced by a cut-down technique from the femoral artery, the carotid artery or the right superficial jugular vein. The arteries were catheterized with a polythene catheter OPP 60 (Portex, England, OD/ID = 1.22/0.76 mm) as described earlier (ADAMS et coll. 1965). The veins were catheterized with a polyvinyl catheter RO I (Portex, England, OD/ID = 1.6/0.85 mm) with three large side holes close to the tip. Small balloon catheters to suit the arteries of the

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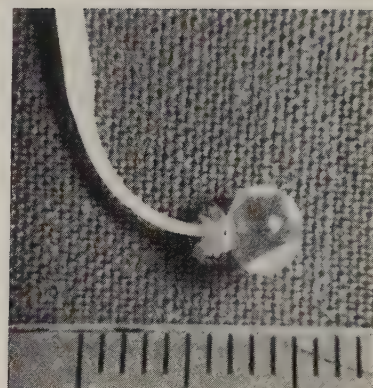


Fig. 1. Balloon catheter of 0.1 ml capacity used in the experiments.

rabbit were made in the following way: a polythene catheter (OPP 60) was heated over a hot air gun (OLIN 1963), tapered, and shaped for the vessel to be catheterized; the end of the tapered tip was then cautiously heated over a flame so that a small flange was produced, a piece of thin rubber membrane (from a condom) being then tied over the flanged tip with Ethicon 4—0 (Fig. 1). Before tightening the knot, the catheter was filled with a water-soluble contrast medium. Different sizes of balloon may be made by this method. If the rubber sheet be stretched across the slightly flanged end, a balloon sufficiently large for the coeliac trunk and the superior mesenteric and renal arteries is obtained. The balloon, due to the elasticity of the rubber, empties as soon as the stopcock at the other end of the catheter is opened. The catheter ought not to contain air or the expansion of the balloon on injection will be unreliable; a small 1 ml syringe is used, the volume that had to be injected to block one of the larger arteries being about 0.05 ml.

Catheters for occlusion or injection were introduced into the vessels with the aid of magnification fluoroscopy. The injection of contrast medium was performed with a high pressure injector (VeReCe, Kistner, Sweden), the flow rate of the injection being recorded on one of the channels of a polygraph by a linear potentiometer. Series of films were exposed with twofold magnification (FFD 90 cm); tube focus 0.3 mm; high definition screens (Rubin, Siemens, Germany) but no grid were used in the film changer (AOT, Elema-Schönander, Sweden) run at suitable speed. Usually 3 to 10 mAs (0.03 to 0.08 s) and 85 to 100 kV gave an adequate exposure with a medium sized rabbit. Contrast medium (Isopaque Cerebral) was injected into a specific vessel at a chosen rate with or without occlusion of another vessel. The following abdominal vessels were examined: the coeliac trunk, the superior mesenteric artery, the hepatic vein, the

portal vein and the renal artery and vein. The vessels in the neck included the right common carotid artery, the innominate artery and the left vertebral artery.

An outline of the different experiments is given below:

Visceral circulation

	Coeliac trunk	Superior mesenteric artery	Hepatic vein	Superior mesenteric vein
Exp. No. 1	Injection	Occlusion	—	—
Exp. No. 2	Occlusion	Injection	—	—
Exp. No. 3	Occlusion	Occlusion	Injection	—
Exp. No. 4	Occlusion	—	—	Injection
Exp. No. 5	—	Occlusion	—	Injection
Exp. No. 6	Occlusion	Occlusion	—	Injection

Renal circulation

	Renal artery	Renal vein
Exp. No. 7	Occlusion	Injection

Cerebral circulation

	Right common carotid artery	Innominate artery	Left vertebral artery
Exp. No. 8	Occlusion	—	Injection
Exp. No. 9	—	Occlusion	Injection

Results

Visceral circulation. When the superior mesenteric artery was occluded and the injection made into the coeliac axis (experiment 1), the diameter of the common hepatic artery as well as that of the proper hepatic artery increased by about 50 per cent and the density of the liver increased (Fig. 2). Small collaterals from the coeliac axis to the superior mesenteric artery were usually evident. The concentration of contrast medium in the portal vein (filled from the gastric veins) increased when the superior mesenteric artery was occluded. No retrograde filling of portal branches from the hepatic artery was observed.

Superselective injection into the common hepatic artery revealed that the caliber of the hepatic arteries was larger and the density of the liver greater than when the injection was made into the coeliac axis. Occlusion of the superior mesenteric artery influenced the appearances to only a minor extent with injection into the common hepatic artery.

The coeliac axis was occluded and the superior mesenteric artery injected (experiment 2). The concentration of contrast medium in the upper part of the portal vein was higher and the ramification of the portal veins in the liver was better demonstrated and wider than in the nonocclusion experiment (Fig. 3).

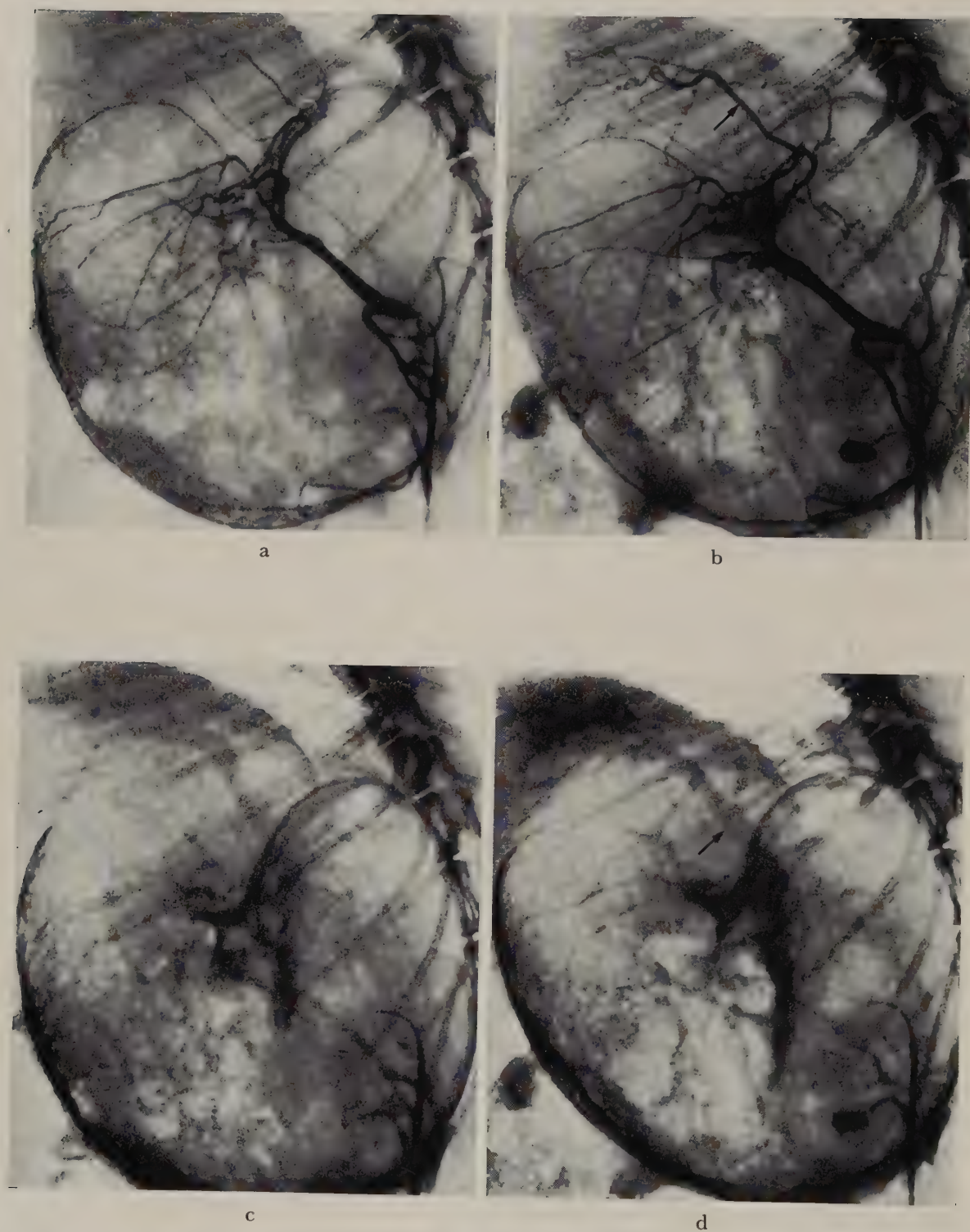


Fig. 2. Coeliac axis angiography. a) Arterial phase. Normal. b) Arterial phase. Balloon occlusion of the superior mesenteric artery. Increased caliber of the hepatic artery ($\rightarrow$). c) Venous phase. Normal. d) Venous phase. Balloon occlusion of the superior mesenteric artery. Somewhat increased filling of the portal venous system and slightly diminished caliber ($\rightarrow$).

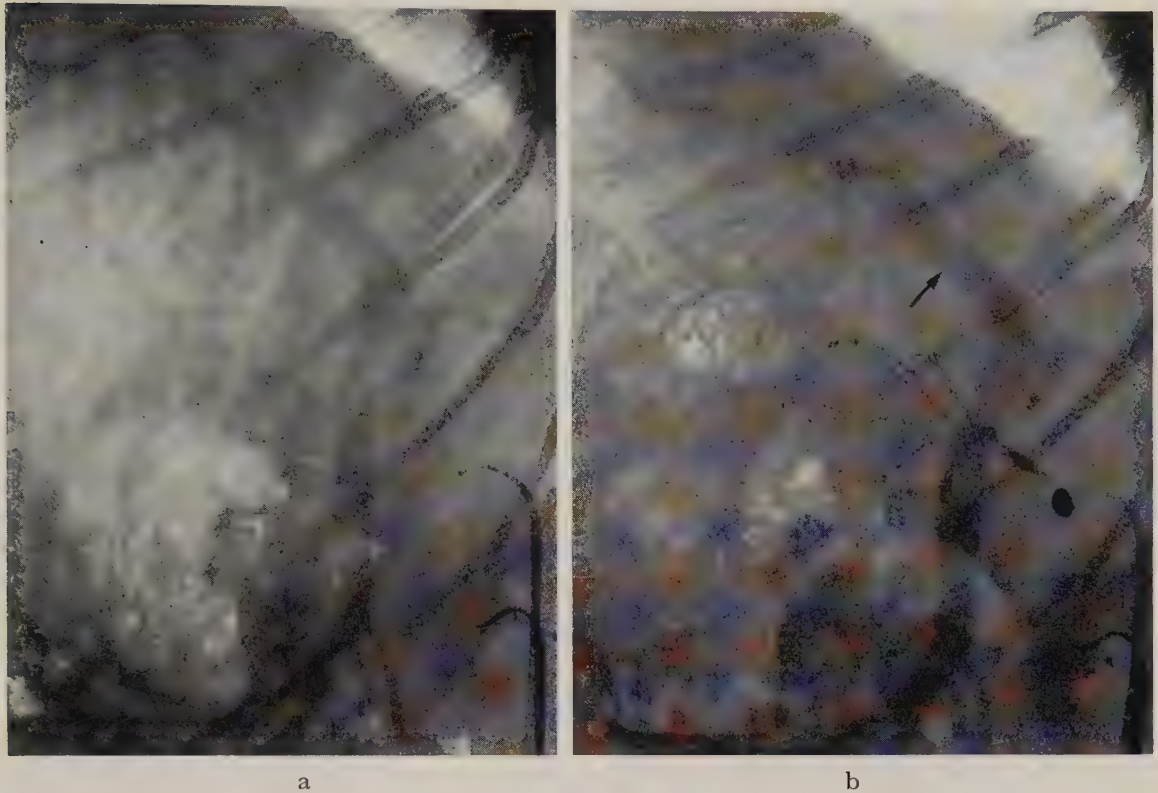


Fig. 3. Angiography of the superior mesenteric artery. Venous phase. a) Normal. b) Balloon occlusion of the coeliac axis. Increased caliber of the portal vein ($\rightarrow$). The coeliac axis is filled with contrast medium through collaterals.

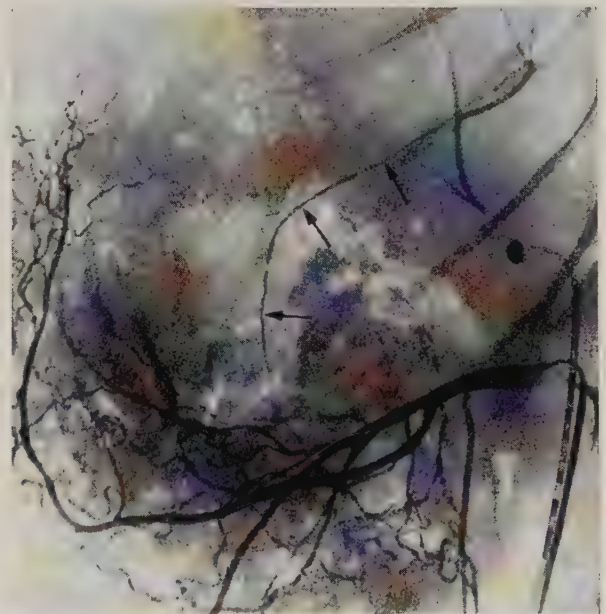


Fig. 4. Angiography of the superior mesenteric artery. Arterial phase. Balloon occlusion of the coeliac axis. Collaterals ($\rightarrow$) to the coeliac axis.

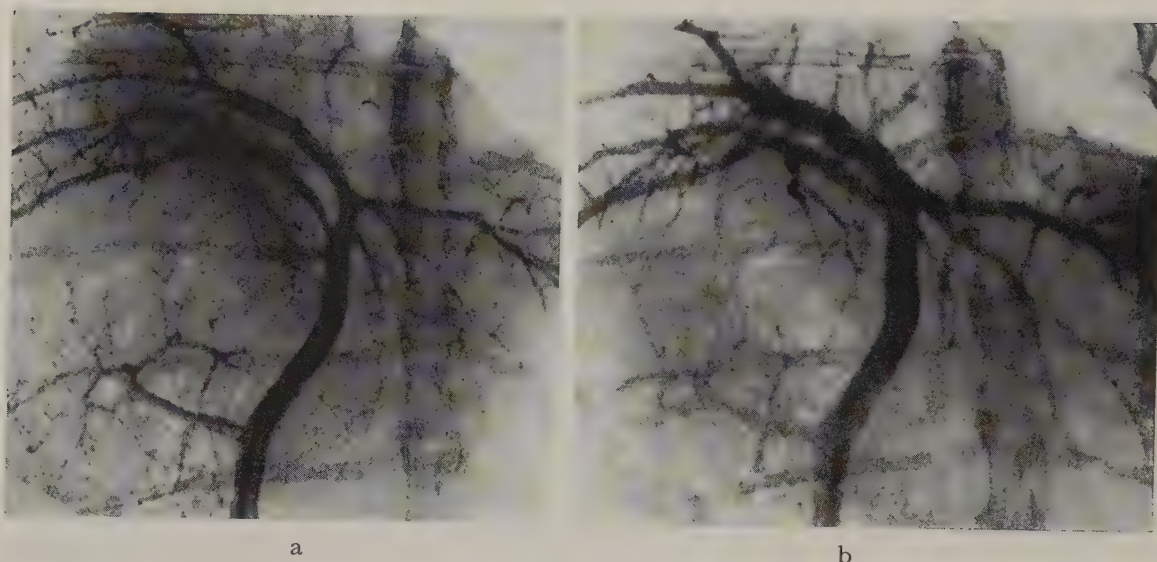


Fig. 5. Angiography of the superior mesenteric vein. a) Normal. b) Balloon occlusion of the coeliac axis. Increased caliber of the portal vein and its branches.

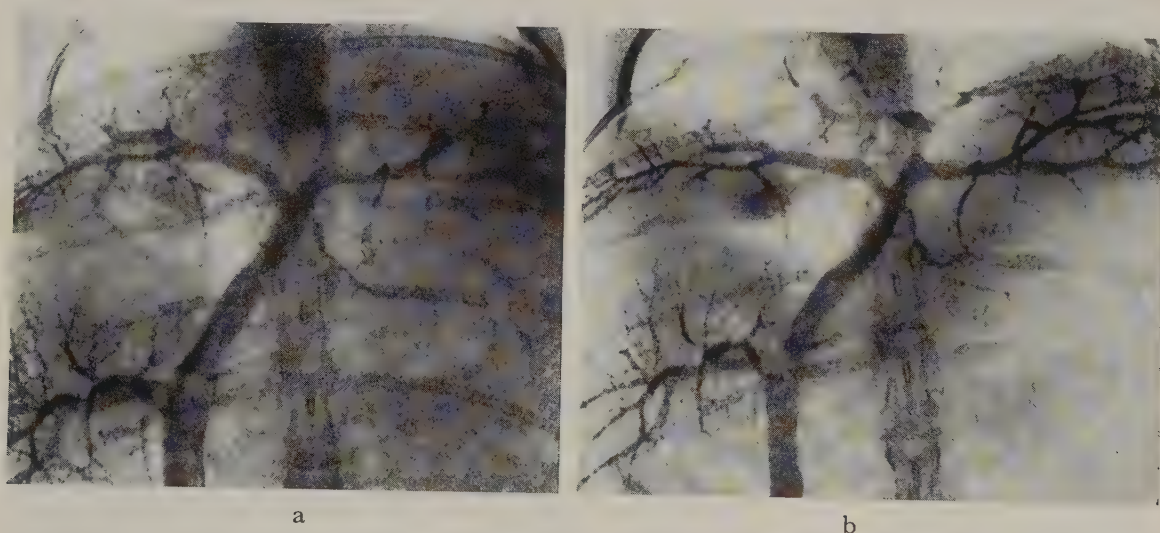


Fig. 6. Angiography of the superior mesenteric vein. a) Normal. b) Balloon occlusion of the superior mesenteric artery. Diminished caliber of the portal vein and its branches.

The filling of the portal system was, however, not as good as in experiment 1. Small collaterals from the superior mesenteric artery to the coeliac axis were usually present (Fig. 4). The caliber of the superior mesenteric artery and its branches failed to change on occlusion of the coeliac axis.

Contrast medium was injected into the hepatic vein at the same time as the coeliac axis and superior mesenteric artery were occluded (experiment 3). The

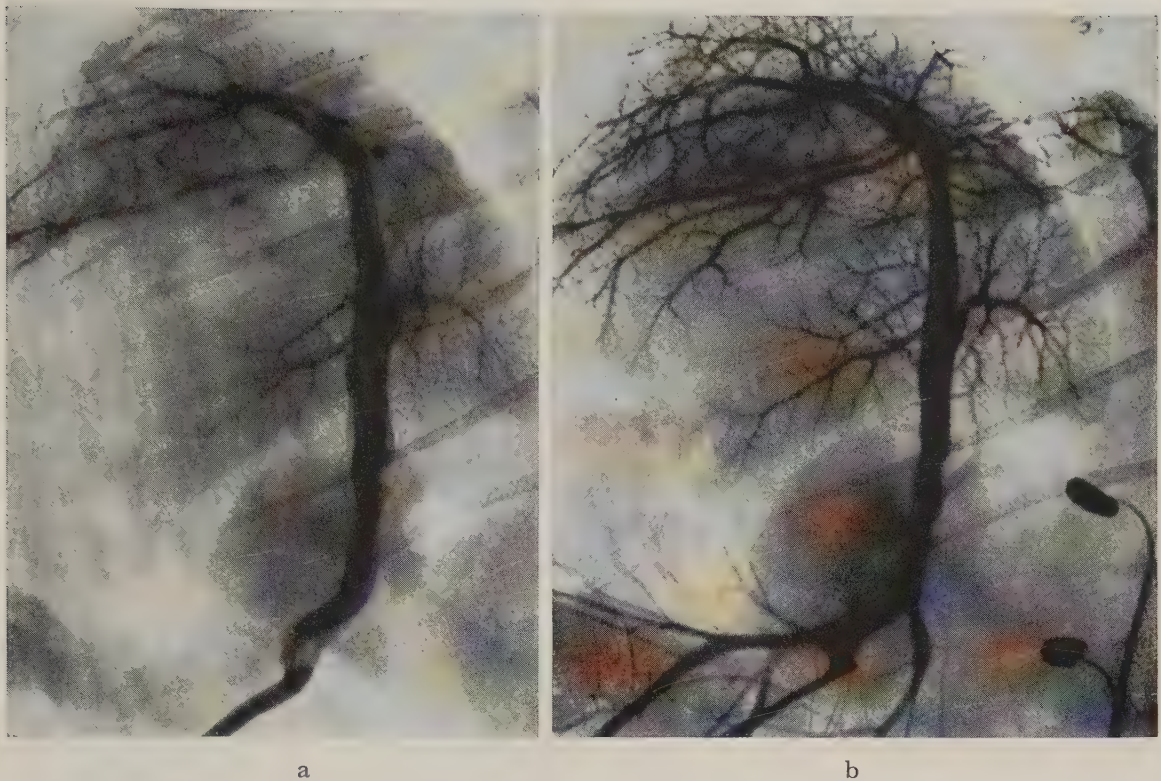


Fig. 7. Angiography of the superior mesenteric vein. a) Normal. b) Balloon occlusion of the coeliac axis and superior mesenteric artery. Much contrast medium in the vein and excellent filling of small branches. Retrograde flow into the superior mesenteric vein.

contrast medium sometimes filled the branches of the vein better than in the nonocclusion experiments. The decisive factor, however, was the position of the catheter in the hepatic vein.

The coeliac axis was occluded and the superior mesenteric vein injected (experiment 4). Less dilution of contrast medium in the portal ramification in the liver was then evident (Fig. 5). No retrograde flow in the mesenteric vein occurred at the injection rates used. The caliber of the portal vein and its branches increased by about 50 per cent on occlusion of the coeliac axis.

The superior mesenteric artery was occluded and the injection made into the superior mesenteric vein (experiment 5). The caliber of the portal ramification in the liver was diminished (Fig. 6). Slight backflow in the superior mesenteric vein often occurred on occlusion of the superior mesenteric artery.

Simultaneous occlusion of the superior mesenteric artery and the coeliac axis, and injection into the superior mesenteric vein formed experiment 6. Practically no dilution of contrast medium occurred and the demonstration even of the fine portal branches was excellent (Fig. 7). Retrograde flow of contrast medium

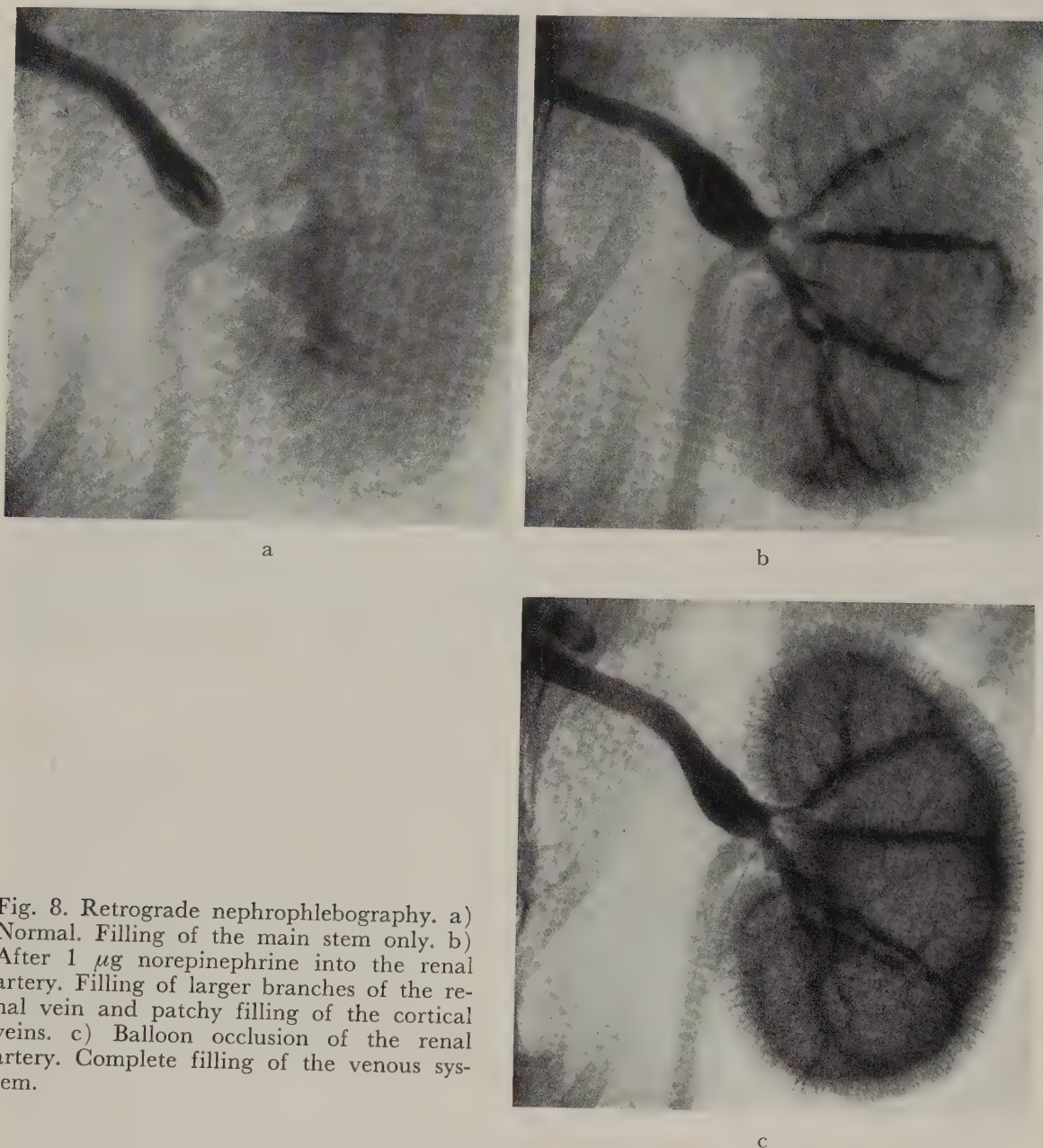


Fig. 8. Retrograde nephrophlebography. a) Normal. Filling of the main stem only. b) After 1 μ g norepinephrine into the renal artery. Filling of larger branches of the renal vein and patchy filling of the cortical veins. c) Balloon occlusion of the renal artery. Complete filling of the venous system.

into the superior mesenteric vein occurred with next to no dilution. The caliber of the portal vessels increased with the rate of injection. The angiogram resembled that obtained on filling of the vessels of a specimen.

Renal circulation. Retrograde injection of contrast medium into the renal vein produced filling only of the first part of the vein stem and sometimes its first branches (Fig. 8 a). If the blood flow through the kidney were diminished by an injection of 1 μ g norepinephrine into the renal artery (20 s before the

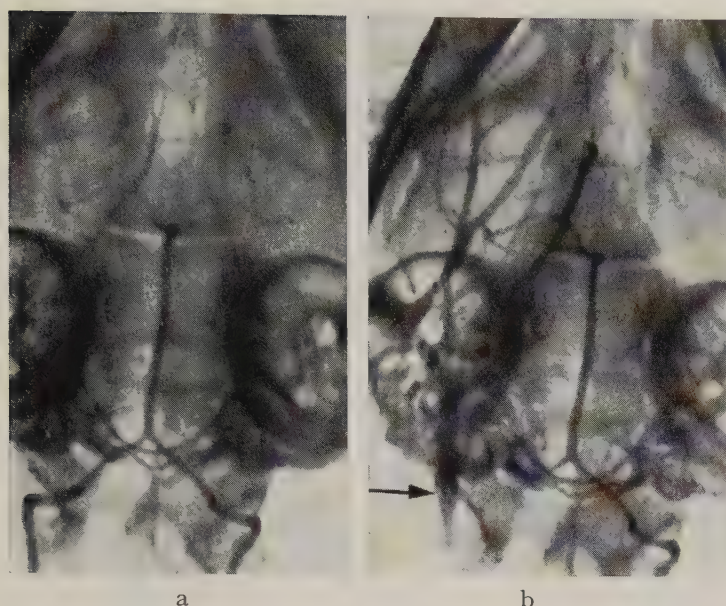


Fig. 9. Angiography of the left vertebral artery. a) Normal. Some retrograde flow into the right vertebral artery. Filling of the posterior part of the circle of Willis. b) Balloon occlusion of the right common carotid artery. Practically no retrograde flow into the right vertebral artery. Filling of the right half of the circle of Willis and retrograde flow into the internal carotid artery to the common carotid artery ($\rightarrow$).

angiography), better filling of the renal vein was obtained (Fig. 8 b). The filling was however patchy and some branches in the periphery remained unfilled. If the injection into the vein were made when the artery was occluded with a balloon (experiment 7), however, complete filling of the venous system out into the cortex occurred (Fig. 8 c).

Cerebral circulation. Injection into the left vertebral artery produced filling of the basilar artery and the posterior part of the circle of Willis. If the speed of injection were high enough, slight retrograde filling of the upper part of the right vertebral artery was also obtained (Fig. 9 a). Occlusion of the right common carotid artery (experiment 8) prevented filling of the right vertebral artery despite an unchanged injection rate (Fig. 9 b). The vascular territory of the right internal carotid artery was outlined via the posterior part of the circle of Willis, and the external carotid artery and its branches were filled through retrograde flow in the internal carotid artery.

If the innominate artery (the common trunk for the right subclavian and right common carotid arteries) was occluded at left vertebral angiography (experiment 9), filling of the posterior part of the circle of Willis was less than in nonocclusion angiography (Fig. 10). Widening of the vertebral arteries and retrograde flow of contrast medium through the right vertebral artery down to the level of the right subclavian artery was evident; from here the contrast medium flowed into that artery as well as up into the right common carotid artery. In one experiment the balloon catheter lay in the right subclavian artery at the origin of the right vertebral artery; retrograde filling of only the upper two-thirds of the right vertebral artery occurred.

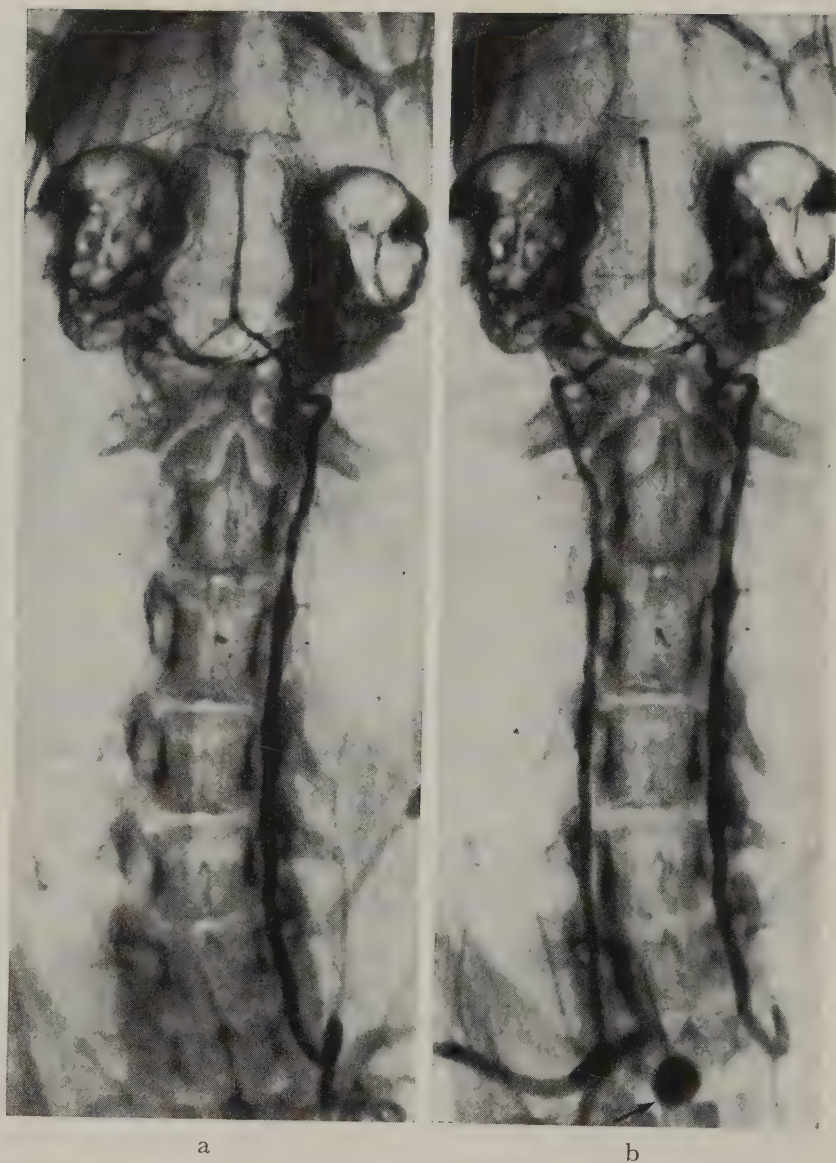


Fig. 10. Angiography of the left vertebral artery. a) Normal. Slight retrograde flow into the right vertebral artery. Filling of the posterior part of the circle of Willis. b) Balloon occlusion of the innominate artery (→). Increased flow into the vertebral artery and retrograde flow into the right vertebral artery down to the subclavian artery. The right common carotid artery is also filled through the vertebral artery. The posterior part of the circle of Willis is not outlined.

Discussion

Visceral circulation. Occlusion of the superior mesenteric artery and injection into the coeliac artery (experiment 1) produced an increase in flow in the hepatic artery which was probably compensatory. GINSBURG & GRAYSON (1954) measured the total blood flow of the liver in rats by a thermoelectric method (internal calorimetry). Occlusion of the portal vein produced a fall in the blood flow to 40 per cent of the original level and then a rise to 50 per cent of the resting flow. SANCETTA (1953) measured the flow in the hepatic artery of the dog with a photoelectric bubble flowmeter; occlusion of the portal vein caused a steep rise in the hepatic arterial flow. SCHWIEGK (1953) obtained the blood flow in both

the hepatic artery and the portal vein of the dog also with a thermoelectric method. He discovered that these flows often reacted inversely; if he diminished the portal flow in one way or another, the flow increased in the hepatic artery. The experiments cited indicate that the hepatic arterial flow will increase when the portal flow is obstructed, which is in accordance with the present angiographic findings. Transillumination investigations of the liver in the frog and rat have disclosed that occlusion of the portal vein fails to stop the flow through the liver (SENEVIRATNE 1949). No reversal of flow from the hepatic artery to the portal vein was revealed at angiography in animals with normal vascular anatomy of the liver. Such a flow has, however, been described in hepatic cirrhosis (CHENDEROVITCH 1956). When the injection of contrast medium was made superselectively into the hepatic artery, the caliber of the artery and its branches rose as compared with when it was made into the coeliac axis (ALMÉN 1966). This probably represented distension of the hepatic artery caused by forced injection. Occlusion of the superior mesenteric artery will not much influence such an angiography.

When the coeliac artery was occluded and the injection made into the superior mesenteric artery (experiment 2), the concentration of contrast medium in the widened portal vein and its branches was satisfactory. This may probably be interpreted as an increase in portal blood flow. GINSBURG & GRAYSON (1954) reported that when the coeliac axis was occluded in rats, the total liver blood flow fell to a mean of 67 per cent of its original level; this was followed by a recovery to a mean of 82 per cent of the original flow within eight minutes after the ligation. REIN (1943) measured the hepatic arterial flow and the portal vein flow in dogs and stated that the portal flow increased when the hepatic artery was occluded. These experiments are in accordance with the present angiographic evaluation. The increased concentration of contrast medium in the portal circulation is probably due to diminished dilution from the splenic and gastric veins brought about by occlusion of the coeliac axis.

Balloon occlusion of the coeliac axis at angiography of the superior mesenteric artery may be tried clinically in the investigation of disease of the portal system. It should be compared to or combined with pharmacoangiography with bradykinin (BOIJSEN & REDMAN 1966). A draw-back of the balloon occlusion method, when the portal venous system is examined from the arterial side, is the increase in the vascular volume of this system which occurs on occlusion of the coeliac axis, which in turn increases the dilution of contrast medium. Before dearterialization of the liver the potential collaterals may be evaluated by preoperative balloon occlusion angiography, e.g. a small amount of contrast medium is injected into the hepatic artery peripherally to the balloon. The washout of contrast medium from the hepatic artery is followed by serial angiography.

One phenomenon on occlusion of an artery that has not been investigated is reactive hyperemia; this latter may be of clinical value. If, for example, the coeliac axis be occluded for five minutes and the occlusion then released, reactive hyperemia occurs (GINSBURG & GRAYSON 1954); contrast medium injected will rapidly be carried away during this phase. Tumour vessels are known to react less to vasoconstrictor agents (ABRAMS 1964) and the same probably holds true for vasodilators. A rapid flow of contrast medium will thus occur from normal structures although not from tumour structures during reactive hyperemia (compare the slow infusion technique for hepatic angiography described by VIRTANEN 1970).

Somewhat better filling of the veins was sometimes obtained by occlusion of the coeliac and superior mesenteric arteries and retrograde injection of contrast medium into the veins of the liver. This increase in quality was not consistently obtained, however, and the method cannot be recommended for clinical application. Retrograde injection of contrast medium into the veins of the liver without occlusion of the arteries has been used in Japan (NAKAMURA *et coll.* 1959, 1969). Better filling of the veins is obtained if the balloon catheters be used on the venous side with occlusion of a segment of the inferior vena cava and injection between the balloons (THALHEIMER & GILLOT 1962). NORHAGEN (1963) tried a variation of this technique utilizing single balloon occlusion of the inferior vena cava at its inlet into the right atrium, combined with compression (increased intrabronchial pressure) of the liver followed by rapid decompression. The balloon occlusion technique on the venous side with one or two balloons is probably the method of choice for examining the hepatic veins. The reason why balloon occlusion of the coeliac axis and superior mesenteric artery rather fails to improve hepatic phlebography is probably largely due to the fact that the pressure in the hepatic veins is low even without occlusion. Of crucial importance, however, is the injection technique on the venous side.

Injection of contrast medium directly into the portal system during occlusion of one or both of the two main arteries (superior mesenteric and coeliac arteries, experiments 4, 5 and 6), produced a decrease in its dilution in the liver and portal system. Occlusion of the coeliac axis caused an increase in caliber of the portal vein and its branches (experiment 4). This was probably compensatory dilatation (compare references cited earlier in this paper; experiment 2). The propagation of contrast medium through the portal system was slowed down and the caliber of the vessels diminished when the superior mesenteric artery was occluded (experiment 5). This was due to diminished flow as well as to decreased pressure in the portal system. The dilution of contrast medium in the portal system at splenoportography would be diminished if the superior mesenteric artery were occluded, and thus a better evaluation both of the collaterals

and of the liver could be obtained. The intriguing haemodynamics of the liver in cirrhosis, hepatoma and other diseases might be evaluated by angiography combined with balloon occlusion of one of the feeding vessels. No backflow from the hepatic artery to the portal vein will occur with a moderate degree of hepatic cirrhosis. If, however, the superior mesenteric artery be occluded, such a flow might be revealed at angiography as an early sign of changed vascular anatomy of the liver. Occlusion of either the coeliac axis or the superior mesenteric artery and injection into the portal system produces excellent angiograms that may be of value if detailed analysis of the liver be desired. The caliber of the portal vein depends on the injection rate and may be altered at will. The method of using a balloon catheter to occlude the coeliac or the superior mesenteric artery may be used therapeutically for arresting bleeding in the oesophagus, stomach and intestines (WHOLEY et coll. 1970). When the blood pressure is lowered locally and the flow velocity diminished, a thrombus may develop in the affected vessel and attach itself to the vessel wall.

Renal circulation. The arterial blood flow to the kidney in retrograde nephro-plebography has to be obstructed so that the contrast medium may be forced out into the small veins of the cortex. The method of HAVERLING (1966) entailing general anaesthesia, increased intrathoracic pressure and balloon occlusion of the aorta and inferior vena cava, is too complicated to be used routinely. The pharmacoangiographic method of improving phlebography by injecting a vasoconstrictor into the renal artery immediately before the injection of contrast medium into the vein (OLIN & REUTER 1965), is much easier to use, although it possesses certain disadvantages. The filling of the small veins of the cortex is often incomplete. In the presence of arteriovenous shunts (carcinoma, arteriovenous shunts, haemangioma) the filling of the shunting veins is also incomplete, as the blood flow through these shunts is not reduced sufficiently by the pharmacologic agents (ABRAMS 1964). Retrograde injection into the renal vein following occlusion of the renal artery by a balloon catheter ought therefore to be a useful method in clinical work, providing that only one renal artery exists. This balloon technique should be compared with occlusion on the venous side (THALHEIMER & GILLOT 1962, TAKARO et coll. 1970). Balloon occlusion of the artery may be of therapeutic value in cases of bleeding from the kidney when no other method can be used, e.g. in inoperable carcinoma (WHOLEY et coll. 1970).

Cerebral circulation. Experiments (8 and 9) indicated that the circulation may rapidly be altered in the vertebral and basilar arterial system and in the circle of Willis. (Compare MACDONALD & POTTER 1951.) The marked increase in the

caliber of the vertebral artery following subclavian artery steal appeared without delay. The experiments described represent a simple means of investigating the principles of collateral circulation and the factors regulating these mechanisms. The occlusion method has been employed for a long time in cerebral angiography to demonstrate aneurysms in different parts of the circle of Willis. Thus compression of the carotid artery on the opposite side is performed to fill an aneurysm of the anterior communicant at carotid angiography and is carried out by digital compression of the vessel. In clinical work, the balloon catheter method would be of value as a test of the capacity of the collateral circulation to the brain before planned occlusion of some of its larger feeding vessels. The method could be used therapeutically to increase the possibility of thrombus formation in an aneurysm by changing the direction of flow and diminishing the velocity of the blood. The advantage of the balloon as opposed to the tourniquet method is the relatively atraumatic nature of the former and the ease with which the volume of the balloon may be adjusted (KESSLER & WHOLEY 1970).

The risks involved in the use of balloon catheters of modern type are fairly small, provided that the period of occlusion be short. If the balloon be over-distended it will change from a sphere to a cylinder, which is easily revealed by fluoroscopy. Undue distension of the balloon may cause vessels to form an aneurysm or to rupture. This will only occur on crude handling, but for safety the authors have started a control investigation in rabbits after deliberately over-distending the balloon in different arteries.

Ischaemia is not well tolerated in the central nervous system, but the collateral circulation via the circle of Willis is effective and if any sign of cerebral ischaemia occurs when the carotid or subclavian artery is occluded it is easy to empty the balloon. The kidney may be deprived of its blood supply for some minutes without any adverse effects (PORCH et coll. 1960). The liver can also tolerate some minutes of ischaemia, especially if arterial collaterals exist and if only one of the main feeding vessels be occluded. The bowel is relatively insensitive to a reasonable degree of ischaemia. Further investigations on the risks of ischaemia when balloon occlusion is used may be carried out by estimating the level of specific enzymes in the blood and urine.

A thrombus may form around balloon catheters, especially if a long piece of catheter lies in the blood stream for some time. This may be prevented by premedication with dextran (Macrodex, Pharmacia, Sweden; JACOBSSON 1968). It is most important that the surface of the balloon catheter should be smooth and even, since a rough surface tends to produce clotting; modern balloon catheters, e.g. those from Edwards Laboratories, California, USA, fulfil these demands. Skilled and careful use of the balloon occlusion technique should not expose the patient to any more risk than ordinary catheter angiography.

SUMMARY

Various arteries in the rabbit have been occluded by balloon catheters. Contrast medium was injected into adjacent vessels and the changed haemodynamics investigated by angiography. The various mechanisms brought into action with this technique are discussed and certain clinical applications are suggested.

ZUSAMMENFASSUNG

Verschiedene Arterien beim Kaninchen wurden mittels Ballonkatheter verschlossen. Es wurde Kontrastmittel in die angrenzenden Gefäße injiziert und die veränderte Hämodynamik mit Angiographie untersucht. Es werden die verschiedenen Mechanismen, die durch diese Technik hervorgerufen werden, diskutiert und gewisse klinische Anwendungen vorgeschlagen.

RÉSUMÉ

Les auteurs ont obstrué différentes artères chez le lapin au moyen de sonde à ballonnet. Ils ont injecté un moyen de contraste dans les vaisseaux adjacents et ont étudié par angiographie les modifications de l'hémodynamique. Ils examinent les différents mécanismes mis en jeu par cette technique et proposent certaines applications cliniques.

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COMPLICATIONS AT BALLOON CATHETER ANGIOGRAPHY

Experiments in rabbits and dogs

R. JENSEN and T. OLIN

Balloon catheters are of value in angiography and therapy (WHOLEY et coll. 1970, JENSEN & OLIN 1972). An evaluation of possible complications has been performed and is now reported.

Material and Methods

The experiments were performed in 6 rabbits and 6 mongrel dogs. In the rabbits general anaesthesia was obtained with intravenous pentobarbitone sodium (Mebumal sodium, ACO, Sweden). A catheter (OPP 60, Portex, England, OD/ID 1.22/0.76 mm) with six side holes close to the tapered tip was introduced into the femoral artery. The contrast medium meglumine metrizoate (Isopaque Cerebral, Nyegaard, Norway) was injected through the catheter by a high speed pressure injector (VeReCe, Kistner, Sweden) and the injection rate continuously registered on a polygraph. Exposure data: FFD 90 cm, nominal focal spot 0.3 mm, 3 to 10 mAs, 0.03 to 0.08 s, and 85 to 100 kV. Rubin high definition screens were used with an AOT film changer (Siemens-Eléma, Sweden). Examinations were made in a.p. and lateral projections. The catheter was then withdrawn and was replaced by a balloon catheter. This catheter (OPP 60) was provided with a home-made balloon at its tapered and bent

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tip, as previously described (JENSEN & OLIN). The major branches of the abdominal aorta were catheterized in turn and the balloon was inflated with about 0.01 to 0.02 ml contrast medium for 2 min. The balloon catheter was then withdrawn and substituted by a catheter shaped for aortography and then by a catheter shaped for selective catheterization of the abdominal arteries. After the angiography had been completed, the catheter was withdrawn and the femoral artery was ligated. About 12 weeks later, a repeat examination was made in 3 of the rabbits, including aortography in two projections and selective angiography of the abdominal arteries. The animals were then killed and the abdominal aorta and its branches were removed en bloc for microscopy.

The dogs had a body weight of 12 to 15 kg and were examined in a similar way as the rabbits. Aortographies were obtained in two projections using a catheter (Ödman-Ledin, Kifa, Sweden OD/ID 1.8/1.2 mm) introduced into the femoral artery. Exposure data: 10 mAs, 0.08 s, 95 to 100 kV. Saphir screens were used. The balloon catheter in this series was a double-lumen catheter (7.5 F, 2.5 mm, Edwards Laboratories, USA) according to WHOLEY et coll. (1970). Before its introduction into the animal, the balloon was filled with contrast medium to make it possible to estimate the size and to control the shape of the balloon. The balloon was inflated with about 0.1 to 0.3 ml contrast medium and deflated after 2 min when positioned in the proper artery. Aortography and selective angiography were performed with the balloon catheter deflated. The incision in the femoral artery was then sutured with silk 6/0. Repeat angiographies were performed 2 to 12 weeks later. Eight ml contrast medium was used for injections into the aorta, the coeliac axis, and the superior mesenteric artery, and 5 ml for the renal artery. Isopaque Cerebral was employed for selective angiography and Isopaque Coronar for aortography. Twofold to threefold direct magnification was used and the diameters of the vessels before and after distension were measured on the films. Magnification adjustment was made with a magnifying glass with a scale graduated in tenths of a millimetre. The diameters were measured in the same way on the repeat films. The measuring procedure was repeated ten times for each film and the mean value calculated for each diameter. As it is difficult exactly to estimate the border lines of the vessels on the film, the error of the diameters were calculated according to the formula:

$$\frac{D}{V} = \frac{A}{C}$$

$$D = \frac{V \cdot A}{C}$$

where D=diameter of the vessel, V=diameter of the vessel measured on the film, A=diameter of the catheter, 1.9 mm, C=diameter of the catheter, measured on the film.

Taking the logarithm and differentiating: $\log D = \log V + \log A - \log C$.

$$\frac{\partial D}{\partial V} \cdot \frac{1}{D} = \frac{1}{V}$$

$$\frac{\partial D}{\partial C} \cdot \frac{1}{D} = \frac{1}{C}$$

$$\frac{\partial D}{\partial V} = \frac{D}{V}$$

$$\frac{\partial D}{\partial C} = -\frac{D}{C}$$

The following formula was used (GRAHN & HERTZ 1971, p. 63):

$$\Delta D = \pm \sqrt{\left(\frac{\partial D}{\partial V} \Delta V\right)^2 + \left(\frac{\partial D}{\partial C} \Delta C\right)^2}$$

$$\Delta D = \pm \frac{1}{C} \sqrt{(1.9 \cdot \Delta V)^2 + \left(\frac{1.9 \cdot V}{C} \cdot \Delta C\right)^2}$$

$$\Delta D = \pm \frac{1.9}{C} \sqrt{(\Delta V)^2 + \left(\frac{V}{C} \Delta C\right)^2}$$

$$\Delta V^2 = \frac{\sum_{n=1}^n 1(V_n - \bar{V})^2}{n(n-1)}$$

$$\Delta C \leq 0.1 \text{ mm.}$$

The edges of the catheter are not difficult to distinguish and the error in the measurement of catheter diameter did not exceed 0.1 mm. The error in the estimation of the vessel and balloon diameters lies between 0.1 and 0.2 mm.

Results

The experiments in the rabbits revealed that there was a very small margin between just sufficient occlusion of an artery and overdilation of the vessel. Little difference existed between the volumes injected and differences in the injection pressure, felt by hand on the piston of the syringe, were imperceptible. The injury was usually greater in relatively small vessels, such as the renal arteries, in contrast to the superior mesenteric artery. The lesion often appeared severe after the balloon was deflated (Fig. 1). Dilatation of the vessel was sometimes evident and a very strong spasm of the vessel occurred distal to the dilatation. Microscopic examination 2 to 12 weeks later revealed injury to the internal elastic lamina and the tunica media. When a marked overdilation had been made, all three layers of the arterial wall could be injured. The 12-week repeat angiography demonstrated regression of the injury to the artery and microscopically a certain degree of healing had occurred. To investigate

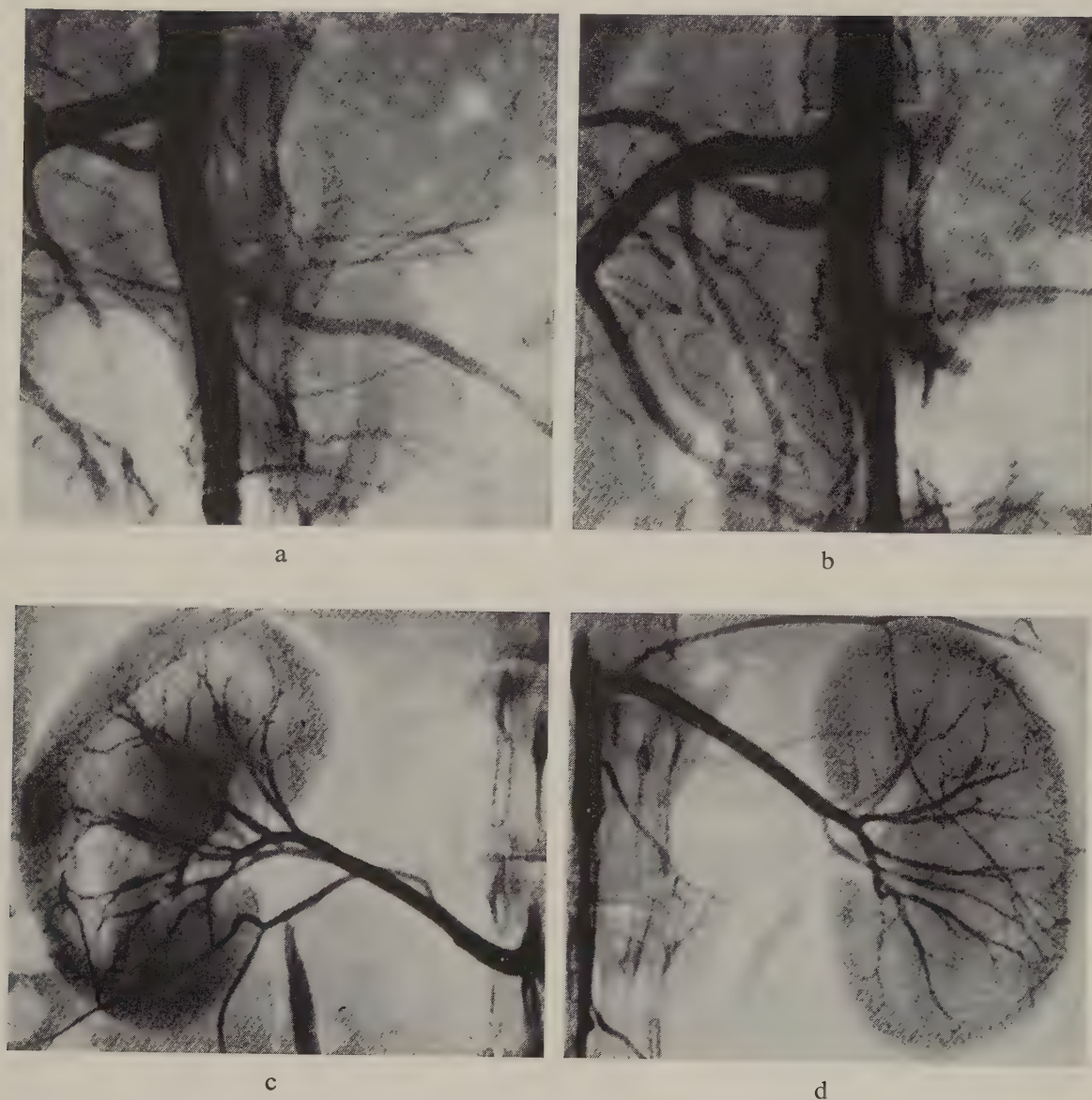


Fig. 1. a) Abdominal aortography of a rabbit before balloon distension. b) Immediately after balloon distension (60–70 %) of the renal arteries. Dilatation of the arteries is partially maintained. Marked spasm of the left renal artery distal to the dilatation. c) Twelve weeks later. Selective nephroangiography on the right side. Normal. d) Twelve weeks later. Selective nephroangiography on the left side. Remaining minimal irregularities of the artery. Microscopy revealed only minor injury to the internal elastic lamina.

whether the preparation of the specimen per se could cause arterial injury, the aorta and its main branches were removed en bloc from a rabbit in which no balloon angiography or selective angiography had been performed. At microscopy lesions were identified in the internal elastic laminae of 2 vessels of 4. Thus, injury to the internal elastic lamina is often secondary to the preparation.

The measurements in dogs are graphically illustrated in Figs 2 and 3. The diameter of the renal arteries, the superior mesenteric artery, and the coeliac axis are demon-

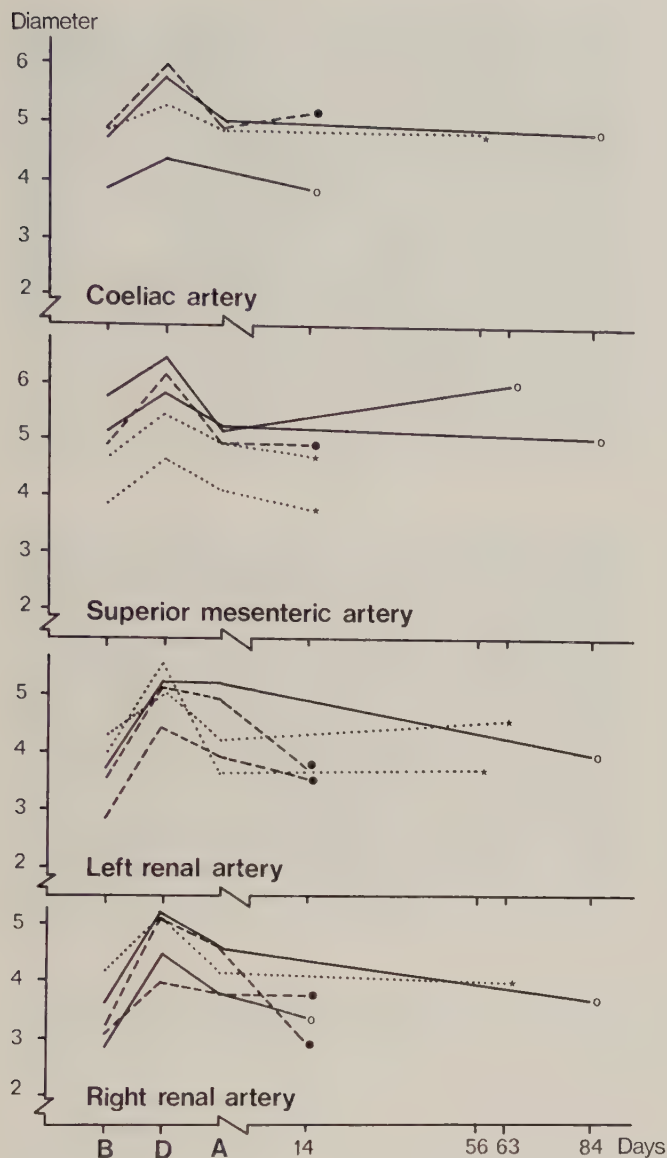


Fig. 2. Diameter (mm) of abdominal arteries in six dogs. B = Before balloon distension. D = During distension. A = After distension. When the balloon is inflated, the caliber increases between 10 and 70%. After deflation of the balloon the vessel often returns to normal caliber. Microscopy after repeat angiography sometimes revealed injury to the vessel wall. ○ = No damage. × = Injury to the internal elastic lamina. ● = Injury to the internal elastic lamina and the tunica media.

strated before, during and immediately after distension with a balloon catheter. The dilatation of the arteries varied. A strong balloon distension of an artery usually diminished or disappeared at exsufflation. Severe overdilation was more apt to occur in small vessels. Thus, it was more common in the renal artery than in the superior mesenteric artery (Figs 4, 5). Major injury revealed at microscopy corresponded to continued dilatation of the artery at angiography. A dilatation was evident in 8 vessels immediately after balloon distension but at repeat angiography some weeks later a small widening remained in 3 vessels only. Microscopy of these vessels revealed rather extensive injury to the internal elastic lamina and the tunica media. In the remaining vessels, where no abnormality was visible on the films, no injury or only small lesions of the internal elastic lamina were identifiable at microscopy. Vascular injury was not common in arteries with an internal diameter of 4

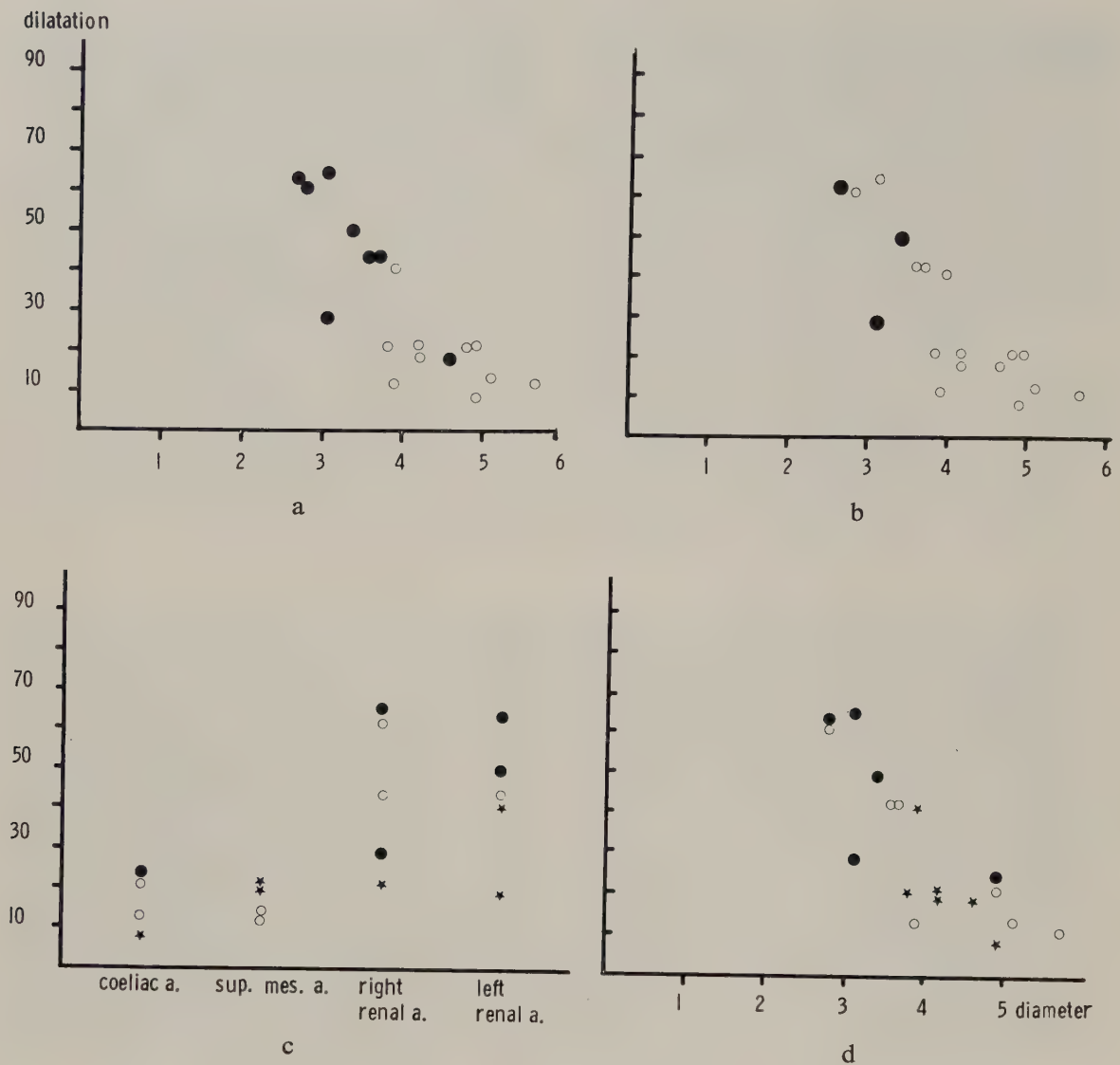


Fig. 3. Diameter (mm) of abdominal arteries in dogs a) immediately after distension by the balloon and b) dilatation at repeat angiography. No dilatation of the arteries apparent when the diameter of the vessel is about 4 mm or more and the distension not over 20 %. At repeat angiography most of the vessels look normal. ● = Dilatation. ○ = No dilatation. c) Dilatation of abdominal arteries and d) degree of microscopic abnormality. In the region without dilatation at angiography, microscopy revealed no abnormality or only injury to the internal elastic lamina. ○ = No abnormality. * = Injury to internal elastic lamina. ● = Injury to internal elastic lamina and tunica media.

mm or more, but was rather common in arteries with an internal diameter of 3 mm or less. Injury to the adventitia was not encountered at any of the experiments in dogs. The repeat angiographies demonstrated that no stenosis of the arteries had developed during the observation period, which extended over 2 to 12 weeks.

In 3 instances the catheter jumped out of a vessel and back into the aorta when the balloon was dilated (Fig. 6). The ellipsoid deformation of the balloon then disappeared although it was sufficiently filled. In these cases the diameter of the balloon

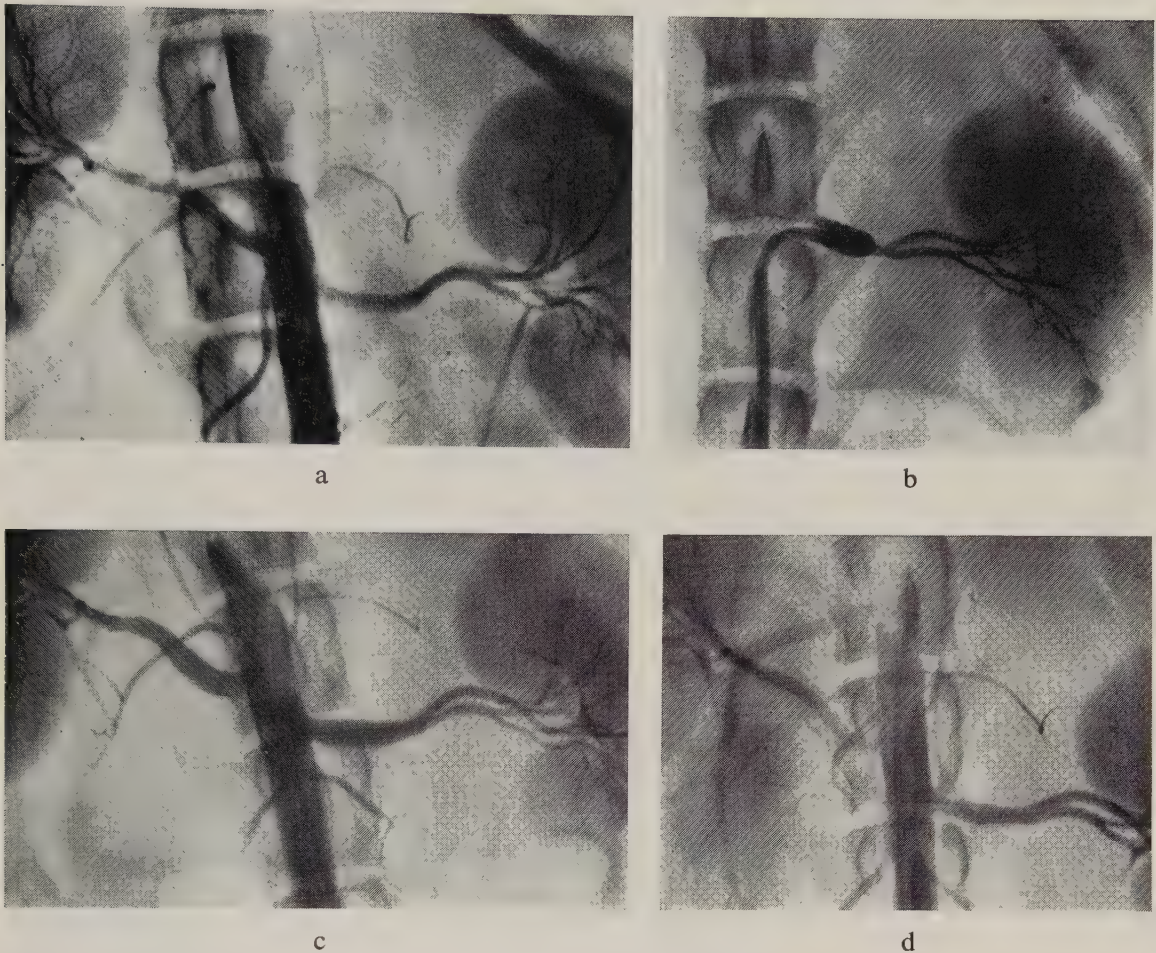
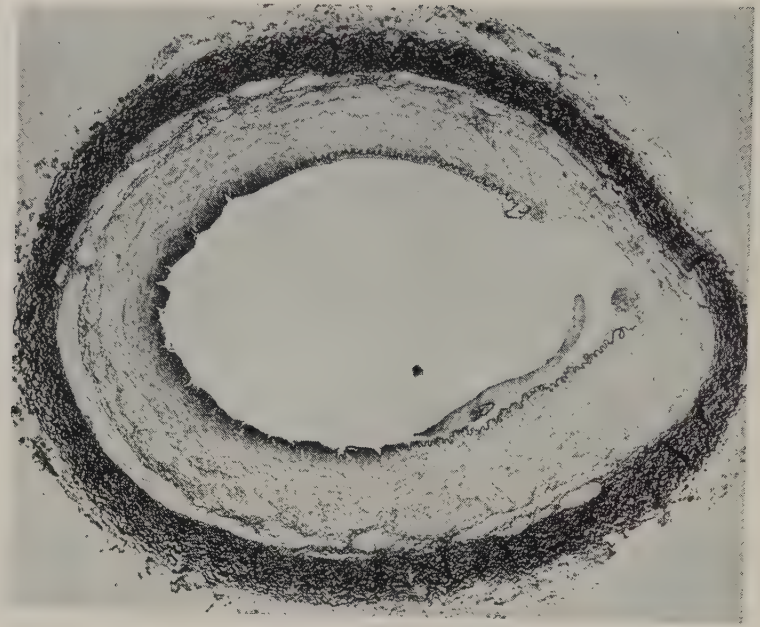


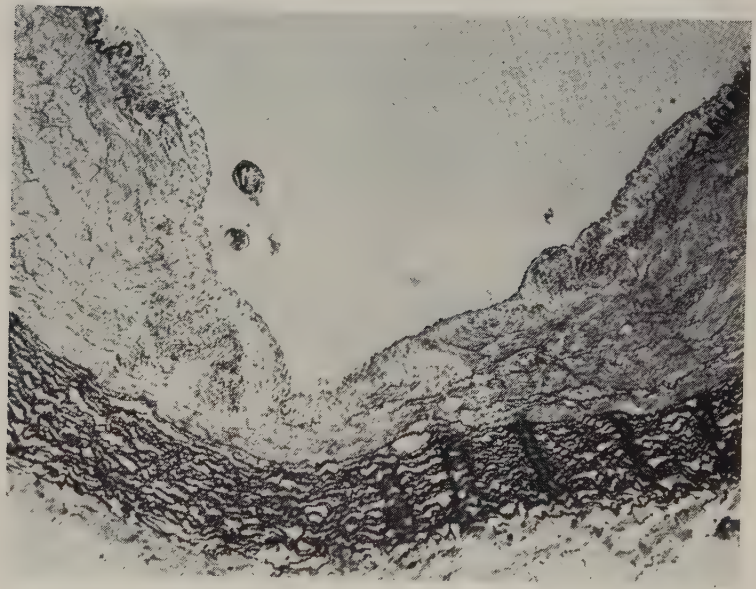
Fig. 4. a) Nephroangiography in a normal dog. b) Balloon catheter inflated in the renal artery. c) Aortography immediately after deflation of the balloon. Smooth widening of both renal arteries by about 50 %. d) Aortography two weeks later. Only slight persistent widening of the left renal artery.

exceeded the diameter of the vessel by between 50 and 90 per cent. Injury to the internal elastic lamina and the tunica media was later revealed in 2 of the 3 arteries although no deformation of the vessels was evident on the films and the distension must have been very brief. No injury was found in one of the 3 vessels, from which the balloon presumably had jumped out during insufflation. The measurements of the diameters of these vessels are not included in Figs 2 and 3.

Direct measurement of the force exerted by the balloon on the walls of a vessel was made as follows: Channels with a diameter of 4.0, 6.0, and 8.0 mm, respectively, were drilled in a piece of acrylic plastic (Fig. 7). The piece was then split lengthwise and a strain gauge was firmly fixed to its top. The balloon was inflated in each channel in turn. The forces exerted on the strain gauge are plotted against the volume injected in Fig. 8. Inflation of the balloon with a very small volume will exert a strong 'expanding' force in a 4 mm channel but only a small force in a 8 mm channel.



a



b

Fig. 5. Same dog as in Fig. 4. Left renal artery. Extensive injury to internal elastic lamina and tunica media. Minor aneurysmatic dilatation. Magnification $\times 40$ and 60 .

Discussion

The blood pressure or an inflated balloon exerts a stress on the arterial wall. The stress, $t_e = (p \cdot r)/t$, where p = pressure, r = inner radius and t = wall thickness. The variation in diameter of an artery with the applied pressure can indicate elasticity, viscoelasticity, or plasticity (BADER 1963). Elasticity implies that a constant relation between pressure and diameter exists, often expressed by Young's modulus of elasticity. When unloaded a perfectly elastic material will immediately go back to the original size. Above a certain load an elastic material will be deformed and will

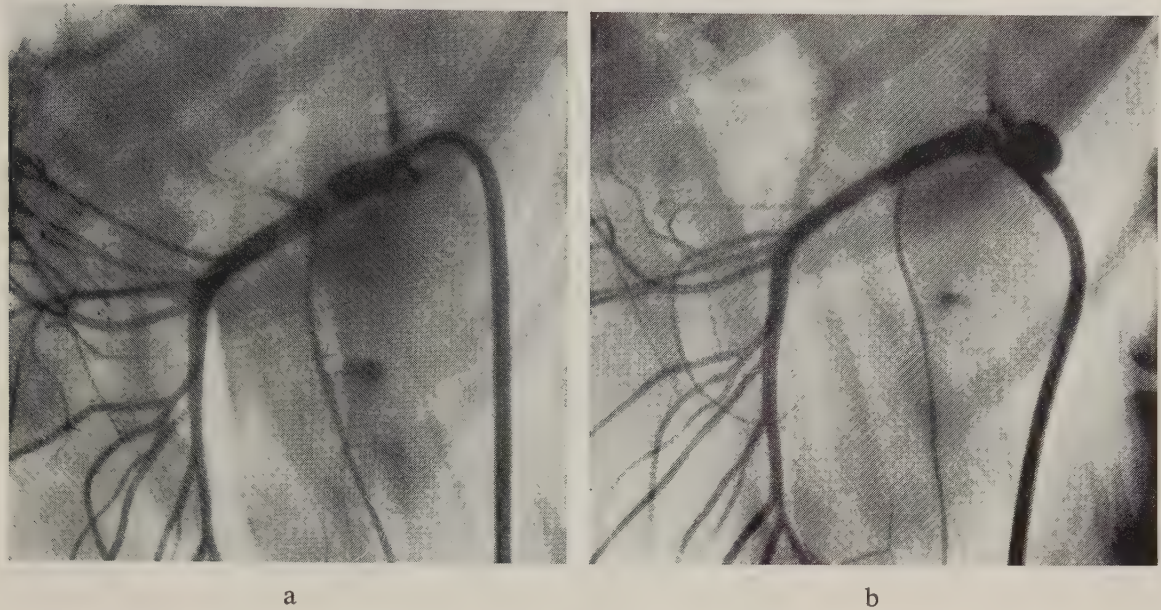


Fig. 6. a) Balloon catheter in superior mesenteric artery of a dog. The inflated balloon is deformed by the artery. b) The balloon has jumped out of the artery into the aorta and regained its spherical shape.

not regain its shape when it is unloaded. Viscoelasticity means that the elastic action is damped by a viscous one. The diameter then depends not only on the pressure but also on the velocity with which it is applied. When unloaded, the material will slowly return to the original size. A material is called plastic when it is deformed on loading and has a tendency to retain its new shape. The arterial wall is not homogeneous but is composed of collagen tissue, elastic tissue and smooth muscles. The proportions of these components vary with species, type of artery, and age. When overloaded the collagenous tissue will behave as a plastic material. If smooth muscles are extended slowly they behave like a plastic material, whereas on rapid extension their response is viscoelastic. Another factor to bear in mind is that the smooth muscles are excited by distension, a response which is considered to account for the so-called autoregulation of blood flow, in, for example, the kidney. Finally the smooth muscles in the vessel wall receive sympathetic and parasympathetic innervation. All these factors must be borne in mind when assessing the effect of balloon catheters on blood vessels.

When a balloon in an artery is sufficiently inflated, it will establish contact about its equator with the inner wall of the vessel. The pressure exerted on the wall is not as great as the pressure inside the balloon, since some of this pressure is counteracted by the rubber membrane of the balloon. On further inflation, the area of contact with the wall broadens and the balloon assumes a shape that to a certain extent is a mould of the artery. The pressure then exerted on the artery is sufficient for distension to occur. At moderate pressures this process is probably viscoelastic and the artery will slowly regain its shape after deflation of the balloon. At higher pressures

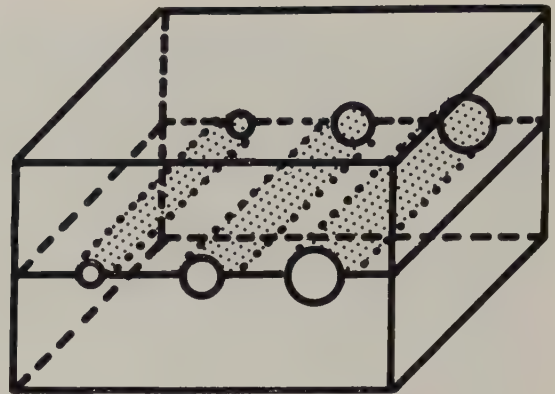


Fig. 7. Piece of plastic with three holes drilled for measurement of the force exerted by balloon catheters.

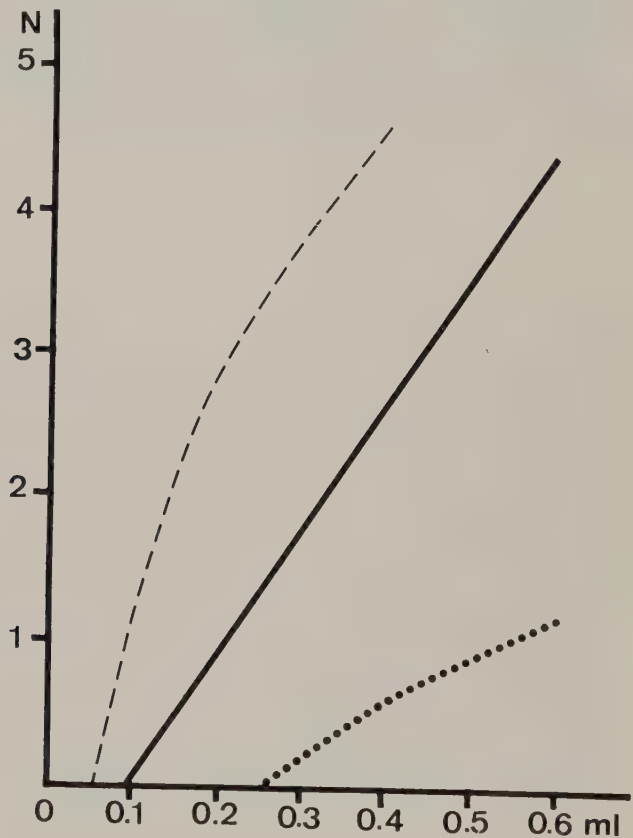


Fig. 8. Force exerted at different degrees of balloon inflation. Diameter: --- 4 mm, — 6 mm, ···· 8 mm.

the distension of the artery will be a plastic process, i.e. dilatation of the artery will be maintained after deflation of the balloon. On distension the smooth muscles in the wall will react to produce constriction; spasm of the artery sometimes occurred immediately after deflation of the balloon.

The volume which has to be injected into a balloon catheter in order to occlude an artery varies with the type of catheter used. The small home-made balloons used in rabbits have a spherical shape. The volume of a sphere is:

$$V = \frac{4\pi r^3}{3},$$

where r = inner radius.

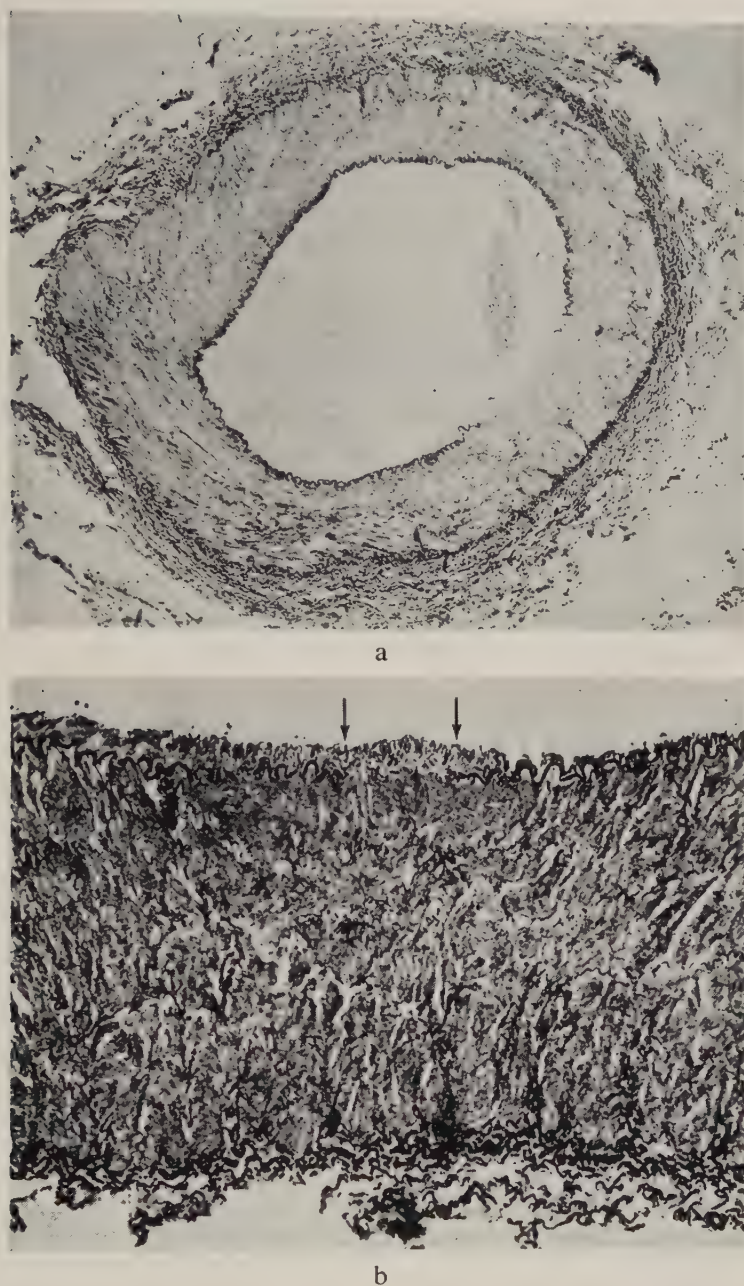


Fig. 9. Microscopy of a renal artery nine weeks after a 20 % distension. Only small rupture of the internal elastic lamina ($\rightarrow$). Similar lesions were also found in vessels which had not been distended. Magnification about $\times 40$ and 100.

The renal arteries of the rabbits used had an inner diameter of about 2.0 mm (mean 2.04). The volume of a sphere which is just large enough to occlude an artery of this calibre is 0.004 ml. Empirically it was found necessary to inject a volume of about 0.01 ml in order to obtain complete occlusion. The difference must be due to minor leakage or to the fact that the catheter contains air, which is compressed when the balloon is filled.

The balloon used in the dogs had another shape, since it was fixed to the catheter at both ends. The volume of such a revolution ellipsoid is:

$$V = \frac{4\pi \cdot ab^2}{3},$$

where a = half the length of the balloon (along the catheter) and b = transverse radius of the balloon. For the catheter in question, $a = 3.1$ mm. The volume of the piece of catheter inside the balloon has to be subtracted and is about 28 mm^3 . The renal artery of a 15 to 20 kg dog has an inner diameter of about 3.4 mm (mean value 3.44, $r = 1.72$ mm). The volume theoretically necessary for occlusion of this vessel is 0.01 ml. In practice, a volume of about 0.1 ml was necessary, and the discrepancy may again be ascribed to air in the catheter and leakage.

Balloon catheters can easily provoke injury to a vessel when they are inflated without care. The risk increases as vessel size diminishes. One explanation for this could be that there is a lesser amount of elastic tissue in relation to the amount of smooth muscles in a smaller vessel. Moreover, experiments in a plastic model demonstrated that a much stronger force was exerted at inflation of the balloon catheter in a small 'vessel' than in a large one. In arteries with a diameter of 4 mm or more the risk is minimal if the increase in the diameter of the vessel does not exceed 20 per cent (Fig. 9). The small injuries to internal elastic lamina might have been produced by the preparation of arteries for microscopy.

It is recommended to estimate the diameter of the vessel at an ordinary angiography in order to minimize the risk of injury. Then, appropriate insufflation of the balloon can be obtained without overdilation of the vessel.

Acknowledgements

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SUMMARY

Overdistension of a balloon catheter may injure an artery and this risk increases with decreasing vessel calibre. Before balloon occlusion an estimation of the calibre of the vessel at a preliminary angiography is recommended.

ZUSAMMENFASSUNG

Überdehnung von Ballonkathetern kann eine Arterie schädigen, und dieses Risiko steigt mit abfallendem Kaliber des Gefäßes. Bevor einer Ballon-Okklusion wird empfohlen, dass der Gefäßsdiameter mit Hilfe einer preliminären Angiographie bestimmt wird.

RÉSUMÉ

La surdistension d'un ballonnet de catheter peut léser une artère et ce risque augmente à mesure que le calibre du vaisseau diminue. Avant d'occlure l'artère avec le ballonnet il est recommandé de faire une angiographie préliminaire.

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DOUBLE-LUMEN BALLOON CATHETER

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Balloon catheters of different types have been described and used for several years. They have often been designed for a specific purpose (NORDENSTRÖM 1962), as flow-guided catheters for determinations of haemodynamics (DOTTER & LUKAS 1951) or as embolectomy catheters for vascular surgery (FOGARTY et coll. 1963, FOGARTY & CRANLEY 1965). However, an all-round balloon catheter suitable for angiography has not been available. Such a catheter has recently been developed in collaboration with A/S Surgimed in Denmark.

Construction. Like the catheters ordinarily used for angiography, the new catheter is made of low-density polyethylene. It is a double-lumen catheter and the inside diameter of the small channel to the balloon is 0.8 mm whilst the large channel which passes through the balloon to the tip has an inner diameter of about 1.4 mm. The outside diameter of the catheter is 2.6 mm except for the thickest part close to the balloon where it measures 3.0 mm. The tip is tapered to an outside diameter of 1.4 mm. The balloon is situated 4.2 mm from the tip, made of latex and fixed to the tube by two small rings of heat-shrinkable polyethylene (Fig. 1). These rings fit into tracks on the catheter to secure the fixation of the balloon. The balloon has a length of 8 mm and is connected to the thin channel in the catheter via two small side-holes. The catheter is normally 90 cm long, but other lengths can be supplied on request. The catheter is disposable and it is not possible to sterilize it in benzalkonium chloride or similar solutions since they will destroy the balloon.

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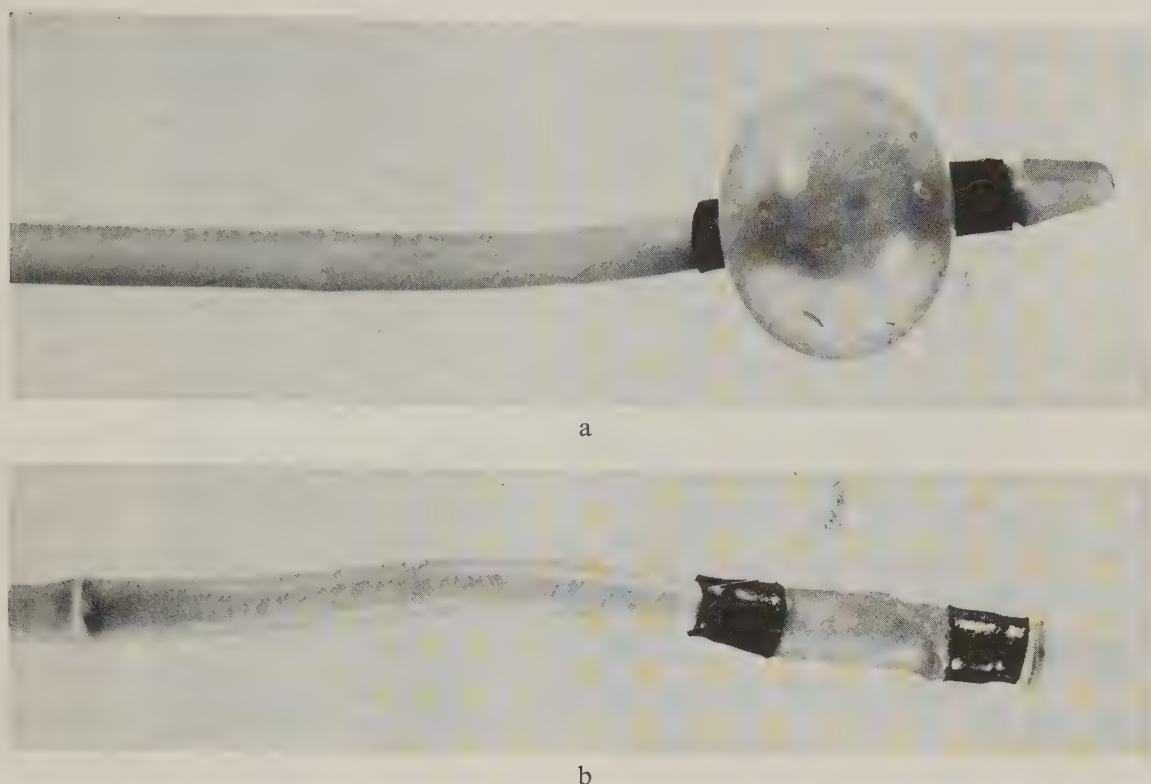


Fig. 1. a) Balloon catheter, inflated. b) When the catheter is straightened out the manoeuvring channel might be kinked off, if wrongly placed on the convexity of the pre-bending.

Technique. The catheter can be moulded in hot water as is commonly done with the ordinary catheters of polyethylene. The catheter should be bent slowly in hot water just below the boiling point and the manoeuvring channel to the balloon should be situated in the inner curve of the catheter. To detect the channel, a copper thread may be introduced into the channel aimed at contrast injection; in strong light the manoeuvring channel can be identified. Another possibility is to observe where the side-holes open into the balloon. If the manoeuvring channel happens to be located in the outer curvature, and the catheter later is stretched out, the channel to the balloon may become kinked, making deflation next to impossible (Fig. 1 b). Before insertion of the balloon catheter, the volume of contrast medium needed for sufficient filling of the balloon, under the conditions at hand, should be estimated. For this purpose a 1 ml syringe, e.g. a tuberculine syringe with a piston diameter of 5 mm, is recommended. The volume normally required for occlusion of some of the larger arteries from the aorta varies between 0.2 and 0.8 ml. That the balloon is sufficiently inflated can be felt on the piston of the syringe when the balloon reaches the wall of the artery. The common technique for percutaneous insertion of a catheter can be used. As a guide-wire a teflon-covered T-160 (A/S Surgimed, 120 cm long) is recommended, as it has low friction against the catheter, contrary to most other guide-wires. The puncture of the femoral artery should not be made at right angles to the vessel but obliquely in order to facilitate the insertion of the catheter.



Fig. 2. Hepatic arteriography with a balloon-occlusion of the artery. No dilution of the contrast medium in the arterial system.

Since the guide-wire is relatively thin the support given to the catheter during the introduction is weak and therefore widening of the puncture hole with a grey catheter (Medioplast 2, soft grey, OD/ID = 2.8/1.4 mm) is recommended. During introduction of the balloon into the desired vascular branch it is often suitable to fill the balloon partially; the bloodstream will then carry it into position.

Application. The catheter has been used experimentally in pigs and clinically in 10 patients. Following its introduction into the femoral artery, different main branches of the abdominal aorta have been catheterized and temporarily occluded. It was also possible to perform superselective catheterization of the hepatic artery. The catheterized artery was occluded for about one minute, i.e. the time necessary for an angiography. When contrast medium was injected peripherally to the occluding balloon, better filling of the arterial ramifications was achieved, facilitating the diagnosis. No reactions from the patients were noted. An angiography after the occlusion was removed, revealed no visible injury to the occluded vessel and no embolization.

One patient (69 years old) developed a haematoma in the groin 12 days after the examination. The haematoma was emptied and the puncture hole in the femoral artery was sutured. Recovery was normal and no further complications occurred. Obviously an atheromatous plaque had been punctured by accident in this case. The caliber of the balloon catheter is somewhat larger than that of ordinary single

lumen catheters and a reduction in caliber is desirable. Only introduction into the femoral artery of adults has been attempted. Catheterization of small arteries such as those of children or the axillary artery of adults, is not to be recommended.

Discussion

Several balloon catheters have been described previously. The USCI catheter, Dotter Lukas No. 1, is rigid and has a very large diameter (DOTTER & FRISEBE 1958). It appears to be intended only for experiments. Edwards Laboratories (USA) make a double-lumen catheter, according to Wholey (GOPALROV et coll. 1972), with a circumference of 7.5 mm (7.5 F). The balloon attachment to the catheter is well made and from experience in dogs and humans, it has proved to be a reliable tool. The shape of the catheter tip is also satisfactory and it is easy to percutaneously insert the catheter into the vessels. The catheter is made of polyvinyl, which makes it possible to glue the balloon, but it has a bad 'memory'. This means that the catheter does not retain a preformed curve after introduction into the bloodstream; it has therefore been reinforced with a steel thread cast into the catheter wall. However, this limits its application and makes it too stiff for several types of work. In our experience it is possible to catheterize only the large vessels and merely close to their origin from the aorta. Another catheter of Edwards Laboratories, the Swan Ganz flow-guided catheter, is available in different dimensions. This catheter is not reinforced and is flexible. It is intended for flow-guided catheterization of the right heart and the pulmonary arteries from a peripheral superficial vein. Selective catheterization of the abdominal arteries with this balloon catheter is next to impossible.

The new catheter described is made of low-density polyethylene, which has a relatively good 'memory', i.e. it will retain a preformed curve relatively well after introduction into the bloodstream. This makes it possible to perform superselective catheterization of the different arteries from the aorta, for example the common hepatic artery.

SUMMARY

Description of a double-lumen catheter with balloon suitable for catheterization and occlusion of different abdominal branches from the aorta.

ZUSAMMENFASSUNG

Die Verfasser beschreiben einen neuen Doppel-Lumen Katheter mit Ballon, der für die Katheterisierung und den Verschluss verschiedener abdominaler Äste der Aorta geeignet ist.

RÉSUMÉ

Description d'un nouveau cathéter à double lumière avec ballonnet destiné au cathétérisme et à l'occlusion de différentes branches de l'aorte abdominale.

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CLINICAL ANGIOGRAPHY WITH BALLOON CATHETER

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Experiments on vessel injuries at angiography with balloon catheter in the dog have shown that injuries seldom occur if the inflation of the balloon is carefully performed and the diameter of the vessel is not increased with more than 20 per cent (JENSEN & OLIN 1979). At such occlusion angiography in the dog and in the rabbit (JENSEN & OLIN 1972) some circulatory changes were demonstrated. The peripheral contrast filling of the arteries was improved as well as that of the veins (WEBER & NOVAK 1980), enabling a better demonstration of abnormalities within the liver and pancreas. These facts could be of value in clinical angiography.

Therefore, the circulation after occlusion of splanchnic arteries was examined in a series of patients and the occlusion angiography was also compared with conventional technique. The intention was to elucidate whether circulatory changes could be useful in diagnosis and therapy.

Material and Methods

Fifty angiographic examinations of the abdominal vessels were made with an ordinary polyethylene catheter (7 F). A double lumen balloon catheter (8 F and 9 F close to the balloon, A/S Surgimed, Denmark) was then inserted according to JENSEN & OLIN (1976) in 33 examinations and a Medi-Tech occlusion balloon catheter (7 F) in 17 examinations. Following inflation of the balloon contrast medium was injected into different abdominal vessels. The age of the patients varied from 27 to 81 years (mean women 63, men 61). The types of angiographic examinations are given in the Table.

The diameter of the vessel to be occluded was measured on the films in the first angiographic series. The diameter of the balloon sufficient to occlude the vessel was then calculated.

In order to find out if the diameter of the inflated balloon was large enough to occlude the vessel without causing injury to the vessel wall the degree of magnification at 54 angiographies was determined. The diameter of the catheter ($OD\ 2.2 \pm 0.06$ mm) was measured on the films. From the true and measured values the magnification of the abdominal vessels was calculated to vary between 1.14 and 1.32 (mean 1.23). Thus, if the diameter of an abdominal vessel is measured on a film the value is about 23 per cent too large. The correct borders of the vessels and catheters were difficult to measure exactly using a magnification glass. Therefore phantom experiments were performed to determine the calculation error of the measurements.

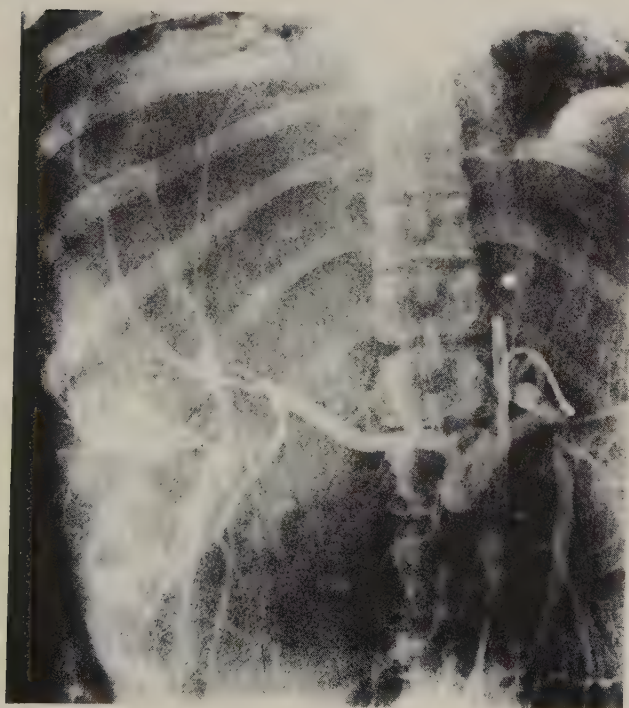
A catheter filled with contrast medium was placed between different blocks of plexiglass. Film focus distance and focus catheter distance were measured in 20 experiments and the correct diameter of the catheters on the films was then calculated. The magnification varied between 1.15 and 1.51, mean 1.29. The difference between the calculated and measured diameter was 0.18 ± 0.02 mm. In 19 of the experiments the calculated diameters were larger than the measured diameters. This means that a vessel is a little wider than what is estimated directly on the film using a magnification glass.



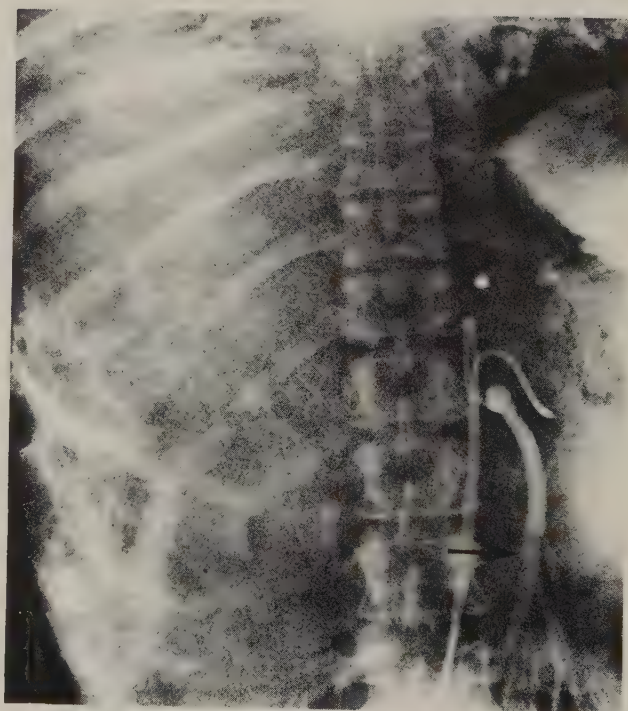
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Fig. 1. Hepatic angiography in a patient with hepatic metastases from a carcinoma of the colon. a) Arterial phase. b) Parenchymal phase. c) Occlusion of the superior mesenteric artery. Arterial phase. Contrast medium is shunted to the superior mesenteric artery via the pancreatico-duodenal arcade. The concentra-

tion of the medium within the hepatic artery and metastases is lower than before the occlusion. d) Parenchymal phase. Contrast medium remains within the superior mesenteric artery close to the balloon. Difference in concentration of the contrast medium in this artery at the entrance of the pancreatic arteries ($\rightarrow$).

Table
Types of examination

Type of examination	No. of cases	Coeliac axis	Hepatic artery	Splenic artery	Superior mesenteric artery
1	6	occl.+inj.	—	—	—
2	2	inj.	—	—	occl.
3	3	—	inj.	—	occl.
4	2	occl.	—	—	inj.
5	3	—	occl.	—	inj.
6	26	—	occl.+inj.	—	—
7	4	—	occl.+inj.	occl.	—
8	4	—	—	—	occl.+inj.

Thus, the error of the measurement did not increase the value of 23 per cent mentioned.

The balloon catheter was bent in hot water with the manoeuvring channel of the balloon along the inner curve to avoid kinking of the channel when the catheter was stretched. The usual technique for percutaneous insertion was used. A teflon covered T-160 guide wire (Surgimed, 120 cm long) was used to fit the narrow injection channel of the catheter. The balloon was expanded with contrast medium of low viscosity (Urografin 30%, Schering AG) to make it easier to empty when the angiography was completed.

The balloon was inflated in the superior mesenteric artery and in different branches of the coeliac trunk. As a precautionary measure the balloon was dilated during fluoroscopy. A deformation of the balloon could then be observed when it reached the wall of the vessel. In the present series the amount of contrast medium injected was 45 ml into the coeliac and hepatic arteries and 50 ml into the superior mesenteric artery. The mean injection rate during conventional angiography of the coeliac trunk and the hepatic artery was 6.6 ± 1.1 ml/s. The rate of injection was almost the same in control series and in those after occlusion, i.e. the injection pressure had to be increased when the balloon catheter was used due to the small inner diameter.

Results

Eight different modes of injection were used (Table). In one group of patients one vessel was occluded with the balloon catheter and contrast medium injected in the same vessel distal to the occlusion (types 1, 6, 8). In a second group one artery

was occluded and contrast injection performed in another vessel (types 2, 3, 4, 5). In a third group (type 7) 2 or 3 vessels were occluded and injection was made in one of the vessels.

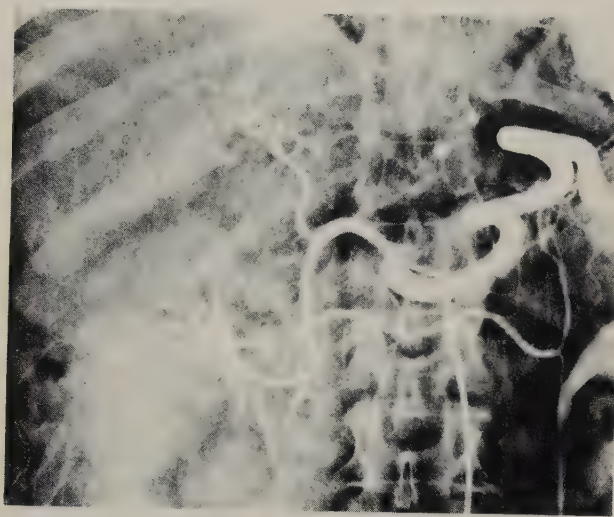
At control angiography immediately after the balloon occlusion no vascular injury was found.

The patients did not experience any inconvenience or pain when the coeliac, hepatic or superior mesenteric arteries were occluded. Some patients experienced a slightly increased feeling of heat when the balloon catheter was used compared with ordinary angiography. This fact was probably due to less dilution of the contrast medium at the angiography with the balloon catheter.

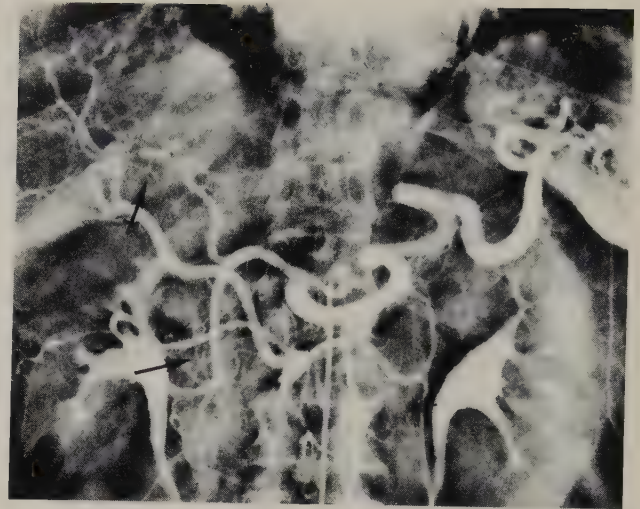
Type 1. Occlusion of the coeliac axis and injection distal to the occlusion gave a complete filling of the branches proximal to the gastroduodenal artery and they were better filled than at an ordinary coeliac injection. Instantaneously blood passed through collaterals in the direction towards the occluded area. The arteries distal to the gastroduodenal artery were thus well filled only when the injection rate (mean 7.5 ml/s, $n=6$) was sufficient to balance the flow from the gastroduodenal artery.

Types 2 and 3. If the superior mesenteric artery was occluded and injection (mean rate 7.8 ml/s, $n=5$) made into the coeliac trunk or the hepatic artery a complete filling was achieved of the superior mesenteric artery distal to the occlusion via the pancreatic arcades (Fig. 1 a, b). The diameter of the vessels of the liver was not changed. Because of vigorous blood mixture and shunting of the contrast medium to the superior mesenteric artery, the filling of the liver vessels as well as the hepatic parenchymal phase were impaired.

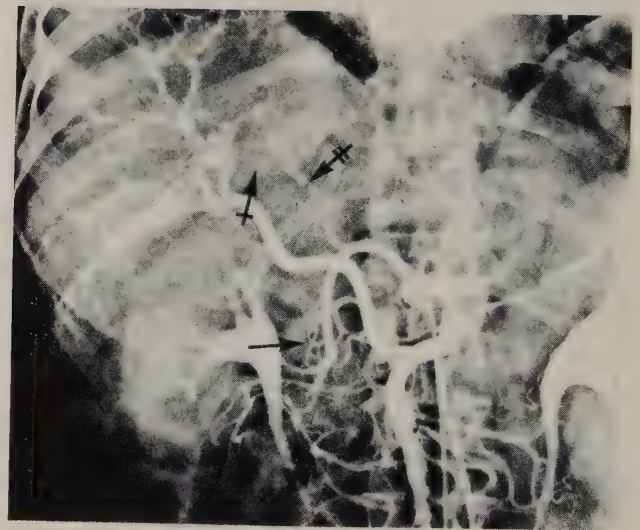
If the right hepatic artery arose from the occluded



a



b



c

Fig. 2. Coeliac angiography. a) Before occlusion of the superior mesenteric artery. No collaterals in the hilum of the liver. b) After occlusion. The pancreatic arteries are well filled as well as the right hepatic artery which originates from the superior mesenteric artery and receives contrast medium via collaterals in the liver hilum (+) and pancreatic arteries (-). c) Angiography of the superior mesenteric artery following occlusion of the coeliac axis. Collaterals in the liver hilum (+) and the pancreatic arteries (-) are well filled in reversed direction of (b). The left hepatic artery is filled from two directions and a small part is not yet visible (+).

superior mesenteric artery this artery was also filled when contrast medium was injected into the coeliac artery (Fig. 2b). This was partly due to collaterals between segmental hepatic arteries and partly to blood flow via the pancreatic arcades which increased in width. The collaterals between the hepatic arteries via the hilum were usually not observed at control angiography (Fig. 2a). The right hepatic artery had the same diameter as when contrast medium was injected into the superior mesenteric artery (Fig. 2c) when this artery was occluded. The portal phase was prolonged at occlusion angiography.

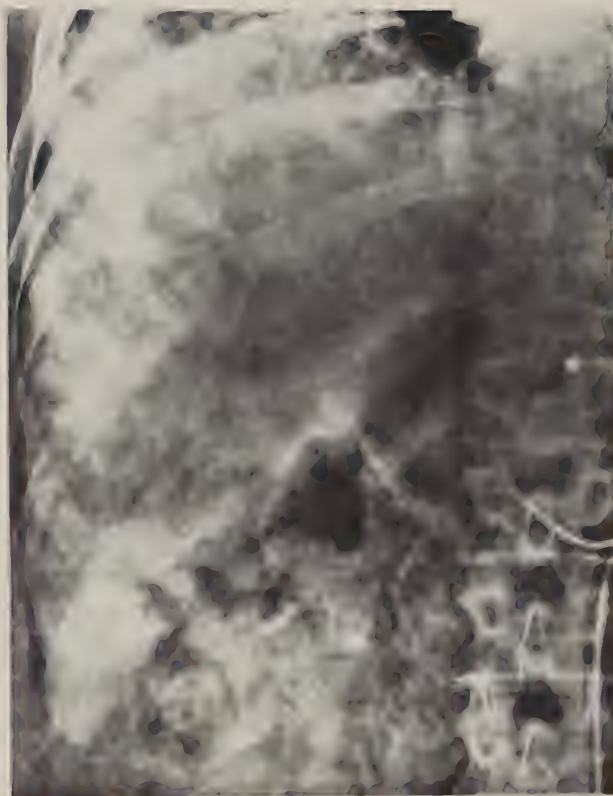
Types 4 and 5. If the positions of the catheters were changed compared with types 2 and 3, so that

the coeliac or the hepatic artery were occluded the flow changed direction both within the pancreatic arcades and within the intrahepatic collaterals between the lobes (Fig. 2c). The left hepatic artery was filled via the collaterals between the lobes. A

Fig. 3. Hepatic angiography in a patient with metastases from a colon carcinoma. a) Arterial, b) capillary phases before the occlusion of the hepatic artery. Injection rate 6 ml/s. c, d) Repeat angiography after occlusion of the coeliac artery. Injection rate 5 ml/s. The direction of flow within the pancreatic and gastroduodenal arteries is reversed and gives a marked dilution of the contrast medium in hepatic arteries with poor delineation of the metastases in the capillary phase. Contrast remaining within the common hepatic artery. Dilution near the balloon (d ↔) indicates collateral flow from dorsal pancreatic artery. Left hepatic artery filled in (a →) but not in (c), because of blood from the left gastric artery.



a



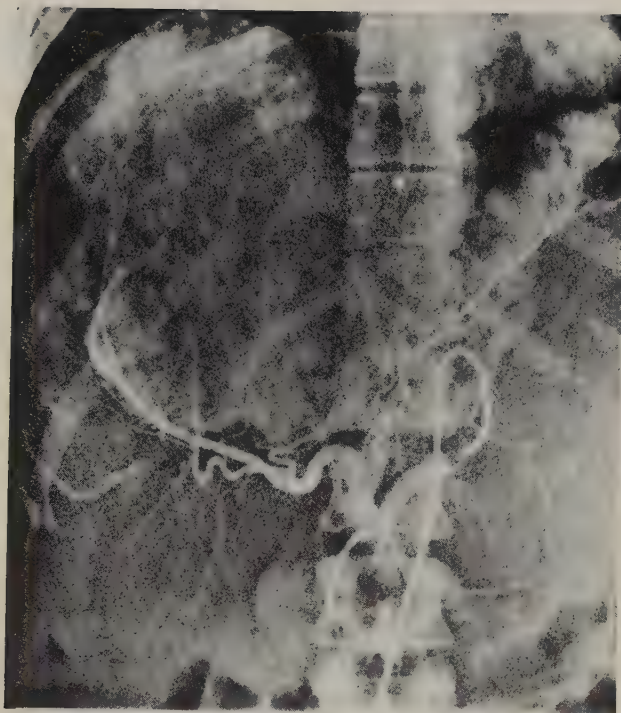
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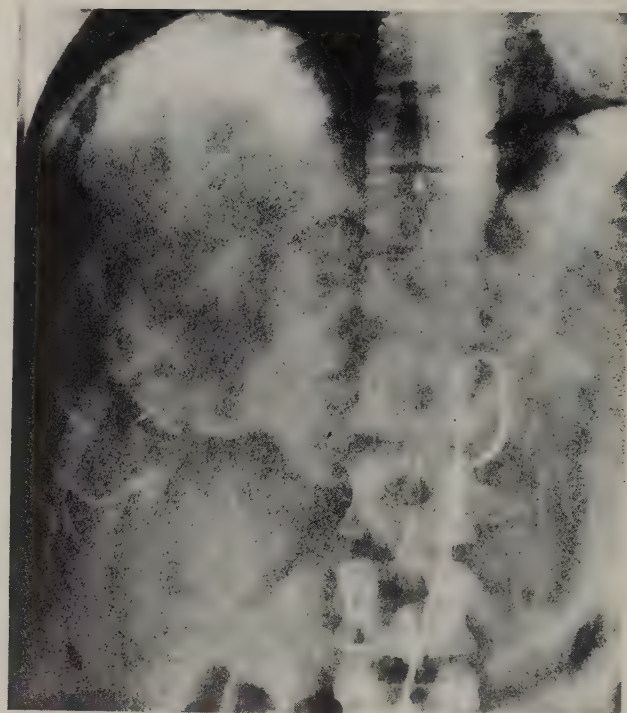
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d



a



b



c



d

Fig. 4. Hepatic angiography in a patient with a large hepatoma. Injection rate 6.5 ml/s, 45 ml contrast medium. a) The arteries in the periphery are not visible. Early capillary phase and high accumulation of contrast medium within the tumour. b) Capillary phase. High accumulation of contrast medium within the tumour and low within the normal part of the liver. c) After occlusion of the common hepatic artery. The injection rate is balanced (6.5

ml/s). The arteries are filled out to the periphery and dilated within the normal part of the liver ($\leftrightarrow$). d) Capillary phase. Less accumulation of contrast medium within the tumour, the concentration of contrast medium within other parts of the liver has increased. A metastasis is now visible in the periphery of the dorsocaudal segment of the right liver lobe ($\leftrightarrow$).



a



b



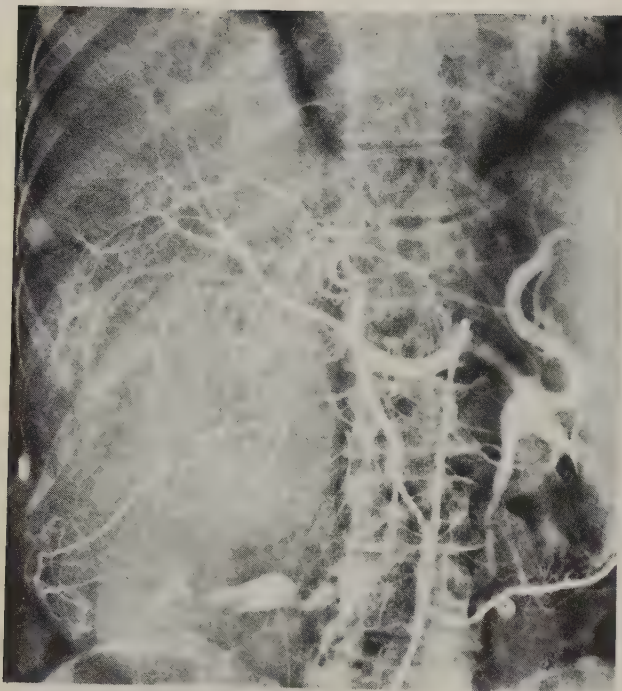
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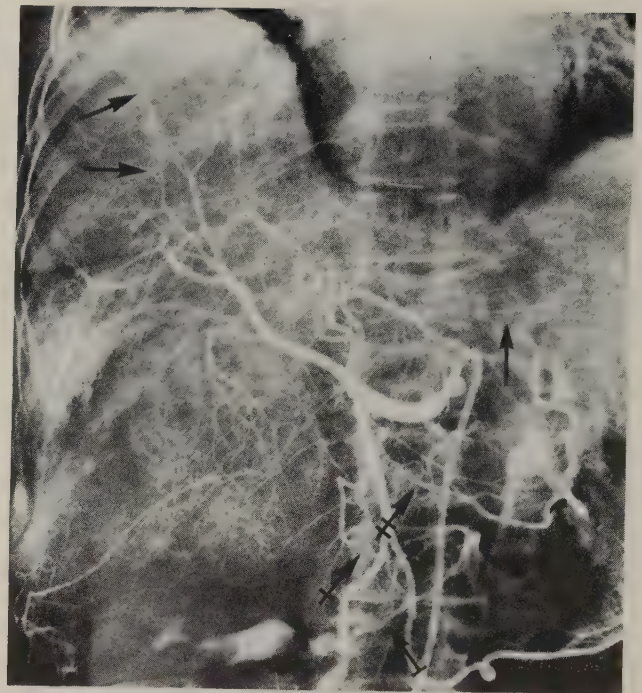
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Fig. 5. Hepatic angiography in a patient with hepatoma. a) Injection rate 11 ml/s in order to obtain maximum filling of the peripheral branches of the hepatic artery and its branches. b) Capillary phase. Poor accumulation of contrast medium within the tumour. c) After occlusion of the common hepatic artery,

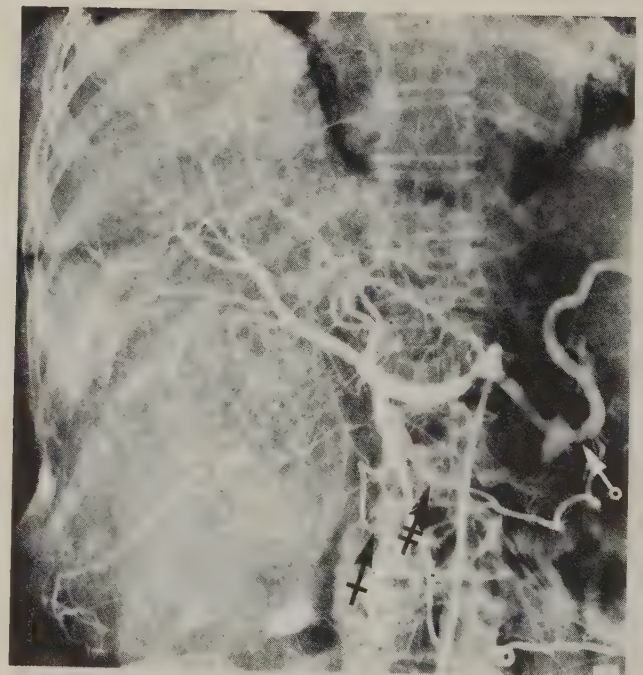
injection rate 8.8 ml/s. The injection has balanced the flow of blood from gastroduodenal artery. Improved filling of the vessels. d) Prolongation of the arterial phase, in particular within the tumour.



a



b



c

Fig. 6. Retroperitoneal sarcoma infiltrating the liver. Hepatic angiography. Injection rate 6.5 ml/s, 45 ml contrast medium. a) Injection before, b) after occlusion of the common hepatic artery. c) After occlusion of the common hepatic artery and the splenic artery. The injection rate caused spill over to the splenic artery (a) and gave an overbalanced injection in (b) and (c). After occlusion the concentration of contrast medium within the vessel has increased and the small arterial branches are visible out to the periphery. Doubling of the arteries ($\rightarrow$) in the liver. Dilatation of the vessels of the pancreas ($+$), the right gastric artery ($\#$); the splenic artery ($\circ\rightarrow$) filled in (c) from the transverse pancreatic vessel.

slight increase of the diameter of the right hepatic artery and the pancreatic arcades occurred. The flow of contrast medium through these pathways gave a good filling of the gastroduodenal artery and the common hepatic artery. The speed of propagation of contrast medium through the splenic artery

decreased because of low perfusion pressure when the coeliac artery was occluded. Compared with control injection into the coeliac artery the contrast medium required approximately the triple time to reach the spleen. The portal phase was prolonged. The width of the portal vein was not changed.

Type 6. When a conventional injection of contrast medium was made into the common hepatic artery contrast filling of the gastroduodenal artery and the pancreatic arcades was often achieved provided that no stenoses were present (Fig. 3a). If the common hepatic artery was occluded proximally to the site of injection the direction of the blood flow through the pancreatic and the gastroduodenal arteries was immediately changed (Fig. 3c). The contrast medium remained within the common hepatic artery if the occlusion was effective. More distally, i.e. within the proper hepatic artery, the contrast medium was quickly swept away by the collateral blood flow from the superior mesenteric artery via the pancreatic arcades.

If the injection rate through the balloon catheter was too low to prevent dilution of the contrast medium with blood from the gastroduodenal artery (below balanced injection rate) the examination gave less information than a conventional angiography (Fig. 3). If the injection rate was increased to balance the flow from the superior mesenteric artery the contrast filling of the liver artery and the parenchyma improved.

At occlusion angiography of the hepatic artery with a balanced injection rate (mean 6.6 ml/s, $n=26$) the diameters of the liver arteries in the periphery were unaltered or increased up to 20 per cent in areas with normal parenchyma. Depending on the injection rate the diameters of the main stems were increased or decreased. In the vessels mainly supplying tumourous tissue no or only a minor increase in calibre occurred at occlusion angiography. The filling of hypervascular tumour was reduced (Fig. 4) and the contrast medium was obviously shunted to areas with normal parenchyma. Within the liver the arterial phase was prolonged about 2 seconds and in areas of tumour infiltration 4 to 6 seconds. In many cases this provided an increased possibility to outline the borders of a tumour (Fig. 5a, b). Also the parenchymal and the venous phases were prolonged and the delay was accentuated within tumours.

When the injection rate was increased so that the collaterals were filled up to the superior mesenteric artery (overbalanced injection rate, mean 8.0 ml/s) the diagnostic information improved. The pancreatic collaterals became wider and were well filled (Fig. 6a, b). The increase of diameter and filling was marked within the vessels filled in the opposite direction to the blood flow. However, the possibilities were limited to improve the arterial filling and the

parenchymal phase of the liver by increasing the rate of injection.

As mentioned the contrast medium was shunted to the superior mesenteric artery via the pancreatic arcades and the only possibility to additionally increase the contrast filling of the liver was to occlude the proper hepatic artery with the balloon, i.e. distal to the origin of the gastroduodenal artery.

The arteries were visible as far out as to the liver surface. About two more ramifications (mean 2.3, $n=26$) were visible. Small pathologic vessels were well filled and in the liver duplication of the arteries was more often seen (Fig. 6b).

Type 7. If both the common hepatic and the splenic arteries were occluded and an overbalanced injection performed into the hepatic artery a filling of the splenic artery via collaterals from the transverse pancreatic artery (Fig. 6c) was observed ($n=4$). If the balloon was adjusted so that the left gastric and also the splenic and hepatic arteries were occluded when injection was made into the hepatic artery, retrograde filling of the left gastric artery to the occlusion site occurred. The splenic artery was filled via collaterals as mentioned.

Type 8. With occlusion of and injection into the superior mesenteric artery proximal to the pancreatic arcade prolonged arterial and venous phases were obtained. At the injection rate of 8.3 ml/s (mean value, $n=4$), the diameters of the branches of the superior mesenteric artery were unchanged. The calibre of the portal vein did not change but the concentration of the contrast medium decreased somewhat. With this type of occlusion and injection no advantages were observed.

Discussion

The risk of complications at balloon catheter angiography may be higher than at conventional angiography. The balloon catheter has often a larger diameter than the conventional ones and the risk of postangiographic bleeding at the puncture site is increased (HALPERN 1964, LANG 1967).

The injection pressure is somewhat higher than at ordinary angiography which increases the risk of subintimal injury. The injection channel has a smaller diameter than in the conventional catheters. The injection pressure is therefore somewhat higher than at ordinary angiography with the same injection rate. The velocity of the contrast medium is raised and the risk of subintimal injury is thus in-

creased. The injection force gives a jet of the contrast medium that could tear off the endothelial layer of the vessel. A reactive force also exists on the catheter in the opposite direction. The reactive force

$$F = \frac{4\rho}{\pi\varphi} \times \frac{Q^2}{d^2}$$

where F = force

Q = flow ml/s

ρ = specific gravity of contrast medium

d = diameter of the tip hole of the catheter

φ = area of jet/area of end hole

(OLIN 1963) is transmitted to the vessel wall by the balloon. The formula proves that the force is proportional to the square of the flow of contrast medium but inversely proportional to the square of the diameter of the tip hole of the catheter. A high injection rate through a catheter and a narrow end hole gives a high force on the vessel wall. Animal experiments have proved such injuries to heal by creating a new endothelial layer (STEMERMAN et coll. 1977) but subintimal dissection and consequent vascular occlusion may occur. This was, however, not observed in the present series. Injury of the vessel wall caused by pressure from the balloon is rare at the degree of dilatation used in the present series if the results from rabbits and dogs (JENSEN & OLIN 1979) are valid in man. At control angiography after decompression of the balloon no lesions were detected. An occlusion of a vessel causes a reduction of the intravascular pressure. As a result the direction of flow in collaterals is diverted towards the area supplied by the occluded vessel. Collaterals usually not seen are widened and take active part in the blood supply (MAYS & WHEELER 1974, LEVIN 1978). Thus the injection rate distal to the balloon must be high enough to make the direction of flow to shift back again in order to demonstrate the peripheral vessels of interest.

Collaterals in the liver hilum between the hepatic arteries can be observed in patients with occlusion of the main stem (REUTER & OLIN 1965, ALMÉN 1966, REDMAN & REUTER 1970). At ordinary angiography GRABBE & LANGE (1981) could demonstrate such vessels in 50 per cent without the presence of arterial occlusion. In the present series, the liver was vascularized from 2 different origins in 6 patients. It was possible to demonstrate the small collaterals at all balloon catheter angiographies but only 4 times with conventional technique. Occlu-

sion of and injection into different vessels (Fig. 2b) gave a good filling of these collaterals.

At the balloon catheter angiography the vessels in the liver and pancreas increased in width and the peripheral contrast filling was improved. Consequently it is quite possible to demonstrate vessels that are usually not visible, e.g. small pancreatic and liver arteries.

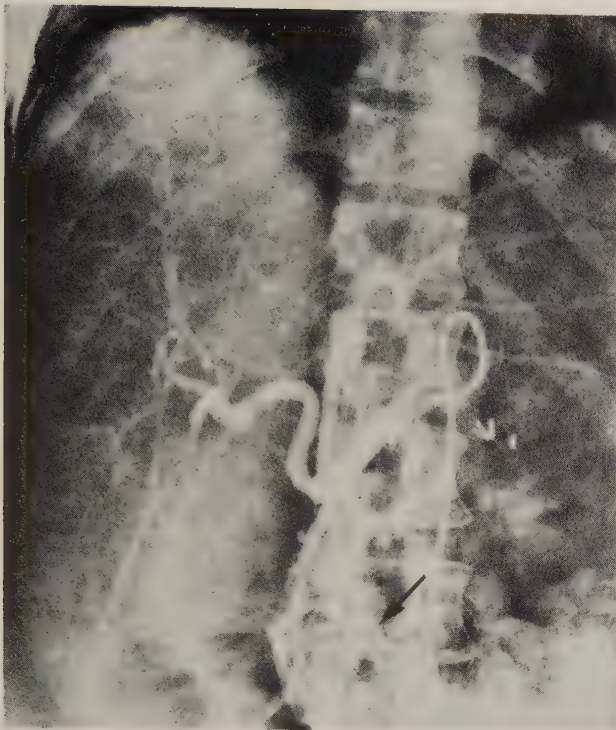
The mechanism responsible for the widening of the vessels after occlusion has been discussed. There are two main theories: the myogenic and the chemical theory.

BAYLISS (1902) observed in arteries from denervated legs from dogs and cats that temporary occlusion was followed by dilatation of the vessels subjected to arrest of blood flow. Vasodilatation occurred also if the occlusion was too short to allow accumulation of vasodilatation metabolites. He suggested the blood pressure to stimulate the vascular wall to a certain degree of tone. This opinion was criticized but BAYLISS (1923) maintained his opinion and was then supported by HIROSE & SCHILF (1931).

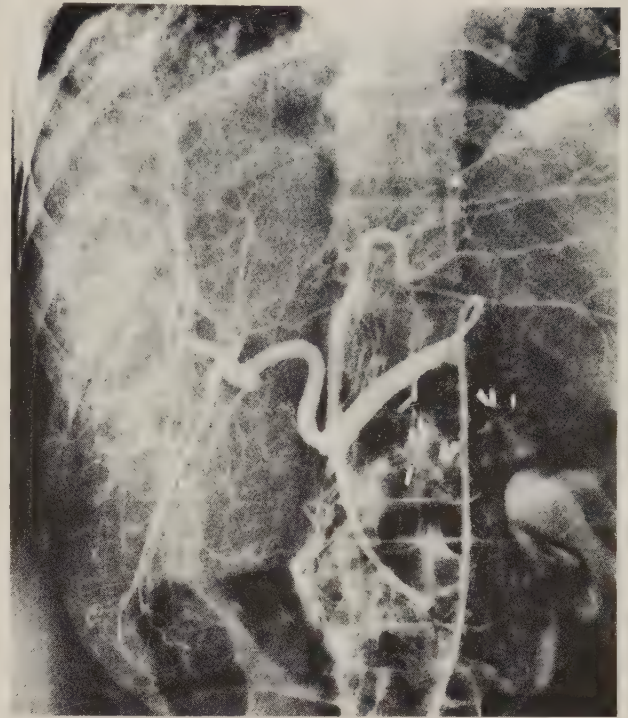
FOLKOW (1949) showed that the blood pressure stimulates the smooth muscles of the small blood vessels to a definite tone. Reduction of the pressure elicits the vasodilatation. In experiments on canine hind limb GUYTON et coll. (1964) showed that vasodilatation occurs when the arterial oxygen saturation was decreased. HIROSE & SCHILF arrested the circulation for 3 to 5 seconds and observed a subsequent vasodilatation. They considered it unlikely that chemical factors were the main cause.

When the contrast injection and the occlusion are made at different sides of the pancreatic arcades the contrast medium and the blood are streaming in the same direction towards the balloon. This type of angiography gives only a slight widening of the vessels and a minor improvement of the filling of small pancreatic vessels compared with ordinary coeliac-superior mesenteric angiography (Fig. 2a, b).

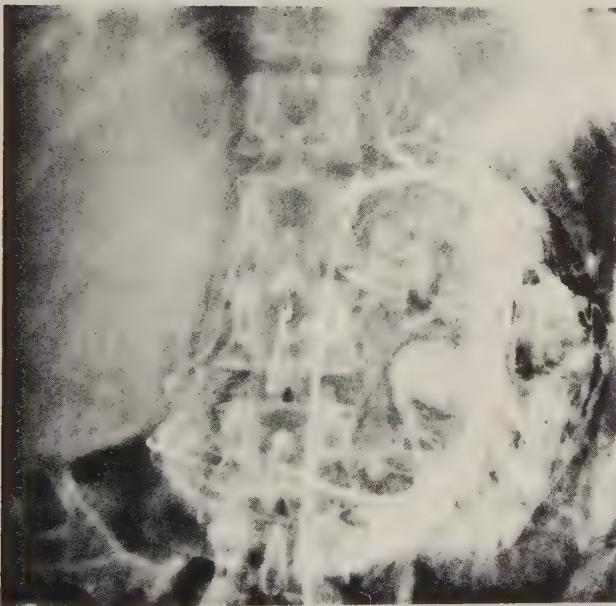
This was also observed by REUTER (1970). A better demonstration of the arteries and the parenchyma of the pancreas is obtained when the injection is against the direction of the blood flow, for instance by occlusion of and injection into the common hepatic artery with a slightly overbalanced injection rate. The mean value for a balanced injection was 6.6 ml/s. If the pancreatic arteries were to be demonstrated, i.e. overbalanced injection, the



a



b



c

Fig. 7. Hepatic angiography in a patient operated upon for tumour in both kidneys. Nephrectomy was made on the right side and resection of the upper pole on the left side. a) Large tumour with blood supply from the right gastric artery. b) After balloon occlusion. Direction of blood flow had shifted in the right gastric artery and as a consequence the contrast medium cannot reach the tumour. c) Left gastric angiography. The collateral and tumour supply is defined.

mean was 7.2 ml/s. It was often necessary to increase this value when the liver was large and required a higher blood flow.

At hepatic angiography with balloon catheter a widening of the peripheral vessels of the normal liver was obtained. The arteries were seen as far out as to the liver surface and small pathologic

vessels could be seen. In the liver with infiltration of a tumour a doubling of the arteries was often seen. However, this can also be observed in the normal liver when a balloon catheter angiography is performed. This is not a sign of tumour growth but an evidence of good contrast filling of small vessels. Injection-corrosion experiments on normal livers have

disclosed small concomitant arteries which pass along and communicate with the major arteries (HALES et coll. 1959, LUNDERQUIST 1981).

In areas with heavy tumour involvement of the liver often no increase in calibre was observed. If a tumour infiltrates a vessel the normal reaction cannot occur. A tumour often induces formation of collagen in the surroundings (PIETRO et coll. 1963, MARIONS & WIECHEL 1974, EKELUND et coll. 1977) and the tissue becomes stiff. This might be the reason for absent dilatation of the arteries even if no evident infiltration of the vessel can be observed. The contrast medium is therefore shunted away from the tumour to areas of normal parenchyma and the filling of a tumour can be reduced at occlusion angiography (Fig. 4).

Dearterialization and infusion of cytostatic agents have been used for treatment of expanding lesions of the liver. Ligation of the hepatic artery induces a dilatation of the vessels in normal liver parenchyma and the cytostatic agent is diverted to the healthy part of the liver and is reduced in a tumour. It can be discussed if cytostatic infusion should be combined with vasoconstriction drugs as vasopressin (SIMMONS et coll. 1977, BOIJSEN & GÖTHLIN 1980) or angiotensin (REUTER & REDMAN 1972) to direct the stream toward the tumour. A balloon catheter angiography should be used as a pre-operative examination to analyze the circulation. It might be more suitable to make an occlusion and an injection of a cytostatic agent with balloon catheter into a branch of the proper hepatic artery.

Collaterals to the liver after ligation of the hepatic artery have been found after a short time (BENGMARK & ROSENGREN 1970, PLENGVANIT et coll. 1972, KOEHLER et coll. 1975). Intermittent occlusion of the hepatic artery prevents collaterals from taking part in the blood supply of the liver. A balloon catheter is practical for intermittent cytostatic infusion as an alternative to surgical treatment before chemotherapy.

At occlusion angiography with injection into the same vessel as the occlusion, the arterial phase as well as parenchymal and venous phases were prolonged. This depends on the decreased regional blood flow within the area supplied by the occluded vessel. The collaterals give a lower pressure (RUSHMER 1970). The decrease of the flow rate is especially marked within the tumour areas where the normal flow is interrupted because of infiltration and stenosis.

WHOLEY (1976) observed that at balloon catheter angiography the contrast medium did not completely push the peripheral blood away in those sites where a partial vacuum was demonstrated. The risk of peripheral thromboses has also been emphasized. In the present series no reduced peripheral filling was demonstrated, provided no powerful flow from any other vessel area had diluted the contrast medium injected. No thrombi were observed either in front of or behind the balloon.

So called 'stand still' or 'stand by' angiograms (WEBER 1979, 1980) were not observed. Only a prolongation with a few seconds of the arterial phase was found. Evidently plenty of communications open up in connection with occlusion (MAYS & WHEELER). If a tumour was supplied by blood from two communicating vessels and occlusion was made in one of the vessels the blood supply came from the other. When occlusion and injection was made in the same vessel the tumour was not filled if the injection rate was low (Fig. 7 a-c). Therefore, it is recommended always to perform an occlusion angiography at high injection rate.

A tumour might be supplied by blood from several vessels (HIETALA & KUNZ 1979, LAMARQUE et coll. 1981). Occlusion of one of the main vessels supplying the tumour and contrast injection into adjacent arteries or into the aorta might give information about the total blood supply and delineate the tumour. Before operation and also when infusion of cytostatic agents is planned it is important to know the total blood supply of the tumour. This is also the case when dearterialization is planned as part of the treatment.

SUMMARY

Balloon catheter angiography of splanchnic arteries demonstrated circulatory changes of value in clinical diagnosis. When the injection rate into the occluded artery was high enough to prevent dilution with blood from collaterals also peripheral arteries were well filled. It was possible to demonstrate vessels usually not visible, e.g. small pancreatic and liver arteries. The arterial phase as well as the parenchymal and venous phases were prolonged at occlusion angiography, which facilitated the demonstration of the outline of tumours.

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PREOPERATIVE EMBOLIZATION OF RENAL TUMOURS USING BALLOON CATHETERS

R. JENSEN and J. NILSSON

Embolization of the renal artery following catheterization and angiography has been described by several authors (ALMGÅRD et coll. 1973, BÜCHELER et coll. 1976, GOLDSTEIN et coll. 1976, ALMGÅRD & SLEZAK 1977, EKELOUND et coll. 1979). Embolization has been used to stop heavy bleeding (CHUANG et coll. 1975, KATZEN et coll. 1976, PROBST et coll. 1980) or as a palliation in the treatment of large renal carcinomas (BÜCHELER et coll., EKELOUND et coll.). The decreased blood flow causes a necrosis within the tumour and it has also been considered that necrosis may cause an increased immunity defense against tumour cells (ALMGÅRD et coll., GOLDSTEIN et coll.). WALLACE et coll. (1981) have presented a thoroughly analysed series of 100 patients embolized with Gelfoam and stainless steel coils.

The aim of the present investigation was twofold: To find out whether preoperative embolization facilitates the operative management of large renal carcinomas and whether the dilatation of the catheter balloon injures the vessel wall.

Material and Methods

Embolization was performed in 13 patients, 6 women (between 50 and 76 years, mean 66) and 7 men (between 44 and 68 years, mean 55). The size and vascularization of the tumour was in all cases demonstrated at nephroangiography. The tumours were measured on the films and the sizes varied

between 5 cm×5 cm and 17 cm×15 cm (mean 12 cm×10 cm). The embolization was performed at a repeated catheterization the day before the operation.

In some cases with tumour supply from lumbar arteries and the superior mesenteric artery only the renal arteries were embolized; in 2 cases with two renal arteries both were embolized. Thus 15 renal arteries in the 13 patients were embolized (left 9, right 6). At operation, the renal artery together with the kidney, was removed, including that part of the renal artery which had been affected by the balloon. Each specimen was examined microscopically.

Three types of balloon catheters were used, manufactured by Edwards Laboratories, California, USA (WHOLEY et coll. 1970), Surgimed A/S, Denmark (JENSEN & OLIN 1979) and Medi-Tech, Massachusetts, USA (WHOLEY 1977).

Surgicel (Ethicon Ltd), a sterilised oxidised cellulose (polyanhydroglucuronic acid), was used as embolizing material. It was cut into very small pieces and mixed with physiologic saline; 1 to 2 ml of the mixture was injected slowly and the catheter rinsed with a few ml of saline. The procedure was repeated and stepwise checked with a few ml of contrast medium at fluoroscopy or exposure of a short series of films.

As the first step the peripheral branches of the renal artery were embolized through an ordinary



a



b

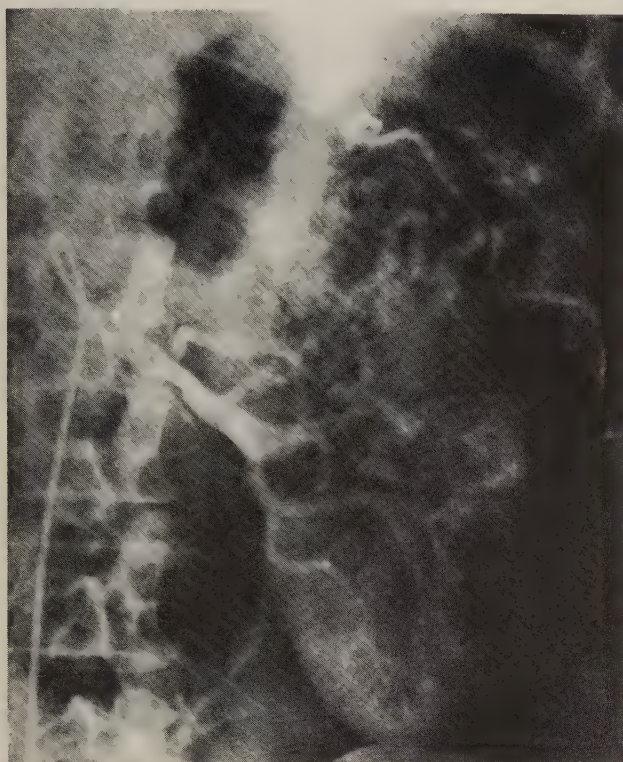


c

Fig. 1. Right-sided renal carcinoma. a) Before embolization. b) After first part of embolization. c) At end of embolization. Contrast medium within the balloon.

angiography catheter with the tip placed well in the renal artery (Figs 1 a, b, 2 a). When the circulation was blocked peripherally the catheter was withdrawn and the balloon catheter introduced. In order

to control the size and form of the balloon the dilatation was made with contrast medium. At a satisfying occlusion the balloon is cylindrically deformed (Figs 1 c, 2 b, c). Through the balloon catheter the central



a



b



c

Fig. 2. Large left-sided renal carcinoma. a) Before embolization. b) Control injection during second part of embolization. Contrast medium within the balloon. c) At end of embolization.

parts of the branches of the renal artery were occluded (Figs 1 c, 2 c). The balloon prevented a reflux of embolizing material to the aorta. With a cautious emptying of the balloon it is possible to observe

contrast medium pulsating in the renal artery as a sign of complete embolization.

A control injection after about 30 min sometimes revealed that the embolizing material had been

Table
Survey of material

Case No.	Age	Sex	Tumour side	Renal artery diameter (mm)	Increase diameter (%)	Duration of occlusion (min)	Microscopic examination of renal artery
1	50	F	R	7.5	25	420	+
2	60	F	L	9	17	600	0
3	63	F	R	8	20	2	(0)
4	72	F	R	8	20	15	0
5	74	F	L	6.5	23	15	+
6	76	F	R	7.5	25	22	0
Mean	65.8			7.8	21.7		
7	44	M	L	5.5	30	5	0
8	45	M	L	{7 8	{28 25	{5 5	{(0) 0
9	47	M	L	10	20	660	0
10	58	M	L	10	20	780	(+)
11	60	M	R	{5.5 5.8	{36 21	{4 8	{0 +
12	64	M	L	8	20	480	(+)
13	68	M	L	10.5	14	60	+
Mean	55.1			7.8	23.8		
Total mean	60.1			7.8	22.9		

+ Injury of internal elastic lamina.

0 No abnormality.

() Dilated part of renal artery, not certainly within operative specimen.

pressed further out into the periphery of the kidney and more embolizing material had then to be injected through the balloon catheter.

The width of the renal arteries, the increase of arterial diameter when the balloon was inflated and the duration of the occlusion are presented in the Table. The duration was varied in order to find out if prolonged occlusion caused increased injury to the arterial wall.

Nephrectomy was performed between 18 and 22 hours after the embolization procedure.

Results

During the embolization procedure the patients had an increasing dull flank pain, in some cases severe. Injection of 10 mg of morphia intramuscularly usually resulted in good pain relief. In one patient an intraarterial injection of 40 mg of lidocain (Xylocain, Astra) was added with good effect. An infusion containing ketobemidon (Ketogin, Lund-

beck) was always administered in order to maintain a painless period.

In some cases a slight fall of the blood pressure occurred in addition to increased pain. Most of the patients had a slight elevation of temperature on the morning before the operation, up to about 38°C. Signs of embolization outside the kidney were not observed.

Findings at operation. All tumours were large ones. In 7 of 8 left-sided tumours splenectomy had to be added to the nephrectomy. In 3 of these cases heavy bleeding occurred from the spleen because of injury to the capsule. The bleeding after embolization was considered as much smaller compared with similar operations without previous embolization. After embolization the kidney and tumour had an appearance similar to that after occlusion of the renal artery at ordinary nephrectomy. This includes a tendency to shrinkage due to decreased blood flow which facilitates the operative management. Thus it was possible to remove even very large tumours.

The postoperative course and the convalescence were without complications.

The operative specimen. At the operation the renal artery was dissected and removed together with the kidney. In some cases technical difficulties were present when resecting the renal artery close to the aorta. In these cases it is possible that the particular part of the artery, which had been dilated by the balloon, was not included in the preparation (Table). Microscopic abnormalities of the vessel wall were seen in 6 arteries and consisted of a slight injury to the internal elastic lamina. The degree and duration of the arterial dilatation in these cases appear in the Table. In 4 of these arteries the intimal injury was at the site of the balloon catheter while this was not confirmed in the remaining 2.

Thrombus formation was observed in all renal arteries. Necrosis of various degree was present within the tumours and other parts of the kidneys. The embolizing material was found within the arterial branches.

Discussion

Embolization of renal arteries has been described by several authors (ALMGÅRD et coll., BÜCHELER et coll., GOLDSTEIN et coll., ALMGÅRD & SLEZAK, EKELEND et coll., CHUANG & WALLACE, 1980, WALLACE et coll. 1981), but no consequently performed series with preoperative embolization in close connection to nephrectomy has been described.

Embolization is usually performed using only one catheter, with or without balloon. In the present series the procedure was divided into two steps with change of catheter in-between.

The first step of embolization is performed with an ordinary angiography catheter without balloon. The inner diameter of this catheter is somewhat larger than that of the injection canal of the balloon catheter which facilitates a more rapid injection of the embolizing particles. As there is no balloon occlusion the full arterial pressure helps to transport the particles out into the periphery of the branches of the renal artery.

As the purpose of preoperative embolization is to reduce the blood loss during the operation it is important that the arterial branches are embolized as far centrally as possible. However, this increases the risk of reflux of embolizing material to the aorta. By changing to a balloon catheter for the second step

of the procedure this risk is excluded also when central branches or the main stem of the renal artery are embolized. Particularly when the renal artery branches off early it may be difficult to avoid reflux without using a balloon catheter. The use of a balloon catheter gives the possibility of injecting embolizing material at high pressure without any risk of reflux (STRECKER et coll. 1979).

Recanalization of embolized arteries has been described by HLOVA et coll. (1976), WALLACE et coll. (1976), BARTH et coll. (1977) and EKELEND et coll. Such a recanalization is probably caused by the pulse wave pressing the embolizing material further out into the arterial branches. This risk of early recanalization can be minimized by leaving the balloon inflated for some hours after the embolization. At the same time a tendency of thrombus formation increases if complete embolization has not been achieved in all arterial branches. A complete occlusion is important in preoperative embolization (BÜCHELER et coll.).

The possibility of embolizing material passing through arteriovenous shunts within the tumour has been discussed (HLOVA et coll., KAUFFMANN et coll. 1980). Such passage of embolizing material cannot be definitely excluded in the present series.

However, despite the embolizing material being injected manually at high pressure, no patients had any clinical signs suggesting such complications.

The material used for embolization was chosen because it is easy to inject in desired amount but the same effect can be achieved with other types of embolizing material as long as no recanalization has occurred before the operation.

One advantage of the used embolizing material is that it is easy to cut into small pieces which facilitates a peripheral occlusion of the vascularity. A peripheral embolization prevents revascularization from collateral vessels (ATHANASOULIS 1980).

The use of metal coils guarantees a definite vascular occlusion and may be the method of choice with a longer delay between embolization and operation (WALLACE et coll. 1981). With as short an interval as in the present series the used material seems to be sufficient.

The effect of embolization has been recorded by the operating surgeons. The degree of blood loss was thus definitely less and the operative procedures were easier than at corresponding operations without previous embolization. This also holds true for very large tumours, previously classified as

non-resectable. A blood loss of lesser degree after occlusion of the renal artery has been emphasized by several authors (MARBERGER et coll. 1974, MARBERGER & GEORGI 1975, BEN-MENACHEM et coll. 1975, HABIGHORST et coll. 1977, REISEGGER et coll. 1977). STECKENMESSER et coll. (1976) also pointed at easier operative procedures.

The balloon compressing the arterial wall did not cause any serious injury despite the fact that the balloon in some cases had been expanded for several hours (Table).

Only slight injury to the internal elastic lamina occurred in a few cases. The type of injury was the same as that in a series of experiments in dogs (JENSEN & OLIN). When the increase of the arterial diameter by the balloon is around or less than 20 per cent as in the present series, only a minor risk of injury of the arterial wall exists. The present experiences are in accordance with those of other authors (OBREZ & ABRAMS 1972, REISEGGER et coll., WEBER 1980, WEBER & NOVAK 1980). However, JEKELL et coll. (1980) emphasize the importance of careful inflation of the balloon in order to avoid complications.

SUMMARY

Preoperative embolization was used in a series of 13 patients for reducing the bleeding during operation of even very large renal carcinomas. During and after embolization pain occurred which necessitated treatment. Balloon catheter embolization was used which excludes the risk of reflux of embolizing material to the aorta. It caused none or only minor injury to the renal arterial wall. No serious complication occurred.

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